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HAEMOLYTIC DISEASE OF THE NEWBORN: CRITERIA OF SEVERITY

BY

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Haemolytic disease of the newborn can now be diagnosed with certainty at the moment of birth by means of the direct Coombs test. However, since this test seems to be positive in all cases of haemolytic disease, criteria are needed to assess the severity of individual cases. Such criteria are not only desirable for the purpose of deciding whether a case requires treatment but are essential for the orderly presentation of data. Of course it is possible to divide cases into the broad classes of hydrops foetalis, icterus gravis neonatorum, and congenital anaemia of the newborn, but close study of the disease reveals every possible gradation between these classes, and any division between them must be arbitrary. Because of this difficulty of grading it is impossible to tell whether different published series of affected infants include similar proportions of severe, moderate, and mild cases; and it is thus impossible to form precise conclusions on the value of different methods of therapy.

Wiener (1946) suggested that the form of anti-Rh in the mother's serum determines the clinical manifestations of haemolytic disease in her infant, but he has recently modified this opinion and now suggests that "blocking" antibodies play the dominant part and that their titre is roughly proportional to the severity of the disease (Wiener and Gordon, 1948); and Davidsohn and Stern (1948) have presented evidence that "blocking" antibodies are associated with more severe forms of the disease than are saline agglutinins. Nevertheless, present opinion has probably been fairly summed up by Diamond (1947): "A prognosis based on antibody tests . . . must be offered with reservations."

Doubtless the search for measurable criteria of severity has been discouraged by the general belief that, in some cases at least, the disease "comes on," or at least increases in severity, after birth. If this were true it would be extremely difficult to make comparisons between cases in view of the variable changes in haemoglobin and bilirubin values that occur after birth as normal phenomena. However, close study of the disease suggests that in fact the haemolytic process is maximal at birth.

This paper presents evidence that the haemoglobin value of the cord blood, determined by an accurate method, is a satisfactory criterion of severity and that knowledge of this value enables one, within limits, to give a reliable prognosis.

Clinical Material

Normal Infants.—In the course of this work cord blood was collected from 52 healthy full-term infants; in addition, venous samples were taken from many of these infants some hours after birth. In 12 of these latter cases the cord was deliberately clamped immediately after the birth of the infant, and in a further 12 cases the cord was left untied for a full five minutes after birth. Finally, capillary samples of blood were taken on the first day of life from a further 33 healthy infants, including 22 from whom venous samples were taken simultaneously.

Infants with Haemolytic Disease.—Seventy-four affected infants were studied, although not all of the tests described below were made on every case. All these infants were born to D-negative mothers whose sera contained anti-D (with or without traces of anti-C or anti-E). In most cases the presence of antibody was first detected by routine tests during pregnancy. Sixty-nine of the infants were born alive, and all were demonstrated to be positive to the direct Coombs test; in a few cases in which the mother had not been tested during pregnancy, and in which the infant was seen by us only after it had developed signs suggestive of haemolytic disease, the diagnosis was first established by the finding of a positive direct Coombs reaction. The blood of five stillborn infants was not tested.

TABLE I

No. of Cases	Hb first Determined	Treatment		
		Nil	Simple Transfusion	Exchange Transfusion
50 { 30	Cord	10 (3 moribund)	1	19
50 { 20	Few hours after birth	0	0	20
17	2–5 days	2	13	2
1	30 days	1	0	0
6	Untested (5 stillborn, 1 moribund)	6	0	0
74		19	14	41

Fifty infants were seen and tested on the day of birth (see Table I), and the findings in this group form the data from which our main conclusions have been drawn. Ten of these infants were not treated—in three cases because they were moribund and in seven because they were considered to be too mildly affected; all of these seven recovered uneventfully. In one further mild case a simple transfusion of Rh-negative blood had to be given on the first day of life because the infant bled from its cord. The remaining 39 cases in this group were treated by exchange transfusion. Thus treatment was essentially uniform, and it seems justifiable to draw conclusions about the severity of the individual cases from the outcome.

In 18 further cases the infant was not tested until after the first day of life. The findings in this group have been used to supplement conclusions reached from the main 50 cases.

Of the 74 cases, 63 formed the material for a previous communication on treatment (Mollison and Cutbush, 1948).

The present paper is concerned with different aspects of the same group of cases and of a further group of cases seen more recently.

Methods

Blood Samples.—Whenever possible cord blood was examined. After tying the cord, blood was obtained with a dry syringe and needle by puncture of the umbilical vein at some point on the placental side of the ligature. When cord blood was not available a venous sample was obtained when the infant was first seen, usually within a few hours of birth. In almost all the cases in the present series, both in normal and in affected infants, this sample was taken by passing a fine plastic catheter up the umbilical vein; 1–2 ml. of blood was withdrawn and rejected before taking the sample for testing. A few venous samples taken on the first day and all those taken subsequently were obtained from a scalp vein, the external jugular vein, or the femoral vein; a scalp vein was used in the great majority of cases. Capillary samples were taken in duplicate from the heel after first warming it in water at approximately 40° C. for at least three minutes.

Determination of Haemoglobin.—Haemoglobin was measured as alkaline haematin in the photoelectric colorimeter; the method employed was essentially that of Wu (1922) as used by Clegg and King (1942). Into 4 ml. of N/10 HCl 20 c.mm. of blood was pipetted. After not less than 40 minutes 1 ml. of N/1 NaOH was added and mixed. (In cases of urgency, alkali was added at the end of 5–10 minutes after tests had shown that this did not lead to lower readings.) The samples were then read in optical cells of a thickness of 10 mm. against a water blank, using a green filter (Chance, O Gr I). During the early part of this work determinations were always made in duplicate, but after an analysis had revealed that the variance of replicate samples taken from venous blood was small only single determinations were made. Since the variance of replicate samples of capillary blood was rather greater, duplicate samples were estimated throughout.

The 20-c.mm., 4-ml., and 1-ml. pipettes used were calibrated and only those having errors within 0.3% of their stated capacity were employed.

The standard deviation of replicate samples was kindly calculated for us by Dr. Cheeseman (of the M.R.C. Group for Statistical Research) from 52 duplicate estimations on venous samples and 102 duplicate estimations on capillary samples. The venous samples had an S.D. of 0.26 from a general mean galvanometer reading of 24.4; this corresponds to an S.D. of 0.17 g. % of haemoglobin. The capillary samples had an S.D. of 0.46 from a general mean galvanometer reading of 25.2.

Haemoglobin Standardization.—The Gibson–Harrison permanent artificial standard (Gibson and Harrison, 1945), obtained from British Drug Houses, Ltd., was used throughout, the solution being boiled for four minutes and cooled before reading. In accordance with a personal communication from Dr. Q. H. Gibson the value of this standard was taken to be 16.1 g. % (in terms of iron) and not 16.0 g. %. As a further check the iron content of a sample of blood was determined by Dr. I. D. P. Wootton, using the "London modified" method described by King *et al.* (1948). This method is claimed to be accurate to within 0.3%. Eight replicate samples of the same blood were tested by our standard colorimetric method. The following results were obtained: Mean galvanometer reading of eight samples, 26.0; reading of Gibson–Harrison standard (boiled and cooled in the usual way and diluted to 2 parts in 5 with distilled water), 25.8. The blood sample is thus estimated to have had a haemoglobin value of 16.2 g. % (the measurements having been made at approximately 18° C.). Dr. Wootton's estimate of the haemoglobin concentration, equivalent to the iron content of this sample, was also 16.2 g. %.

Plasma Bilirubin Estimations.—The method of Haslewood and King (1937) adapted for the photoelectric colorimeter (King, 1947) was used, with the important modification (King and Wootton, 1948) of diluting the plasma with buffer if the readings were found or expected to exceed one and a half times the standard. This modification leads to considerably higher readings than those given by the original method and no doubt goes a long way towards meeting criticisms of the method (e.g., Gray and Whidborne, 1946). It is not yet known whether this modified precipitation method still gives lower results than the method of Malloy and Evelyn (1937). Determinations were always made upon venous samples; haemolysed plasma samples were discarded.

Serological Tests

(*a*) *Direct Coombs Test* (Coombs, Mourant, and Race, 1946).—After washing the erythrocytes three times in saline a 10% suspension (approx.) was prepared and one drop of this was mixed with one drop of anti-globulin serum on a flat opal tile. After half a minute the tile was slowly and gently rocked over a lighted box and examined with the naked eye for agglutination. If no definite agglutination developed within six minutes the test was considered negative. It was noted that different anti-globulin sera varied greatly in potency, and the reagent in use was tested from time to time as follows:

Normal Rh-positive cells were incubated with a serum known to contain only a trace of anti-Rh; the cells were then washed and tested against the anti-globulin serum. Even with potent reagents the reaction was never strong, and with moderate or weak anti-globulin sera there was no reaction at all. Through the generosity of colleagues we were fortunate in being able to maintain stocks of anti-globulin sera which would agglutinate such weakly sensitized cells.

The anti-globulin sera had been absorbed with human erythrocytes of different groups and were always diluted with saline to 1 in 20 or 1 in 50, depending upon their strength; they were nevertheless tested against washed unsensitized cells of different groups from time to time to see that they did not give non-specific agglutination. Occasionally when these tests were being read it was noted that a faint granularity developed after about 10 minutes' rocking on the slide, even though it was known that the cells were unsensitized. For this reason the convention was adopted of discounting any reactions developing after more than six minutes' rocking.

(*b*) *Indirect Coombs Test.*—Two volumes of serum were incubated at 37° C. with one volume of a 20% suspension of known O Rh-positive cells (usually CDe/CDe) for not less than 30 minutes. The cells were then washed and tested as above.

(*c*) *Titrations in Saline and Albumin.*—The technique of Boorman *et al.* (1942) was used for saline titrations. For albumin titrations the sera were diluted in 30% bovine albumin and tested against cells suspended in 20% albumin (Diamond and Denton, 1945). Readings were made in conformity with the technique described in M.R.C. Memorandum No. 19 (1948).

(*d*) *Rh-testing.*—Mothers and infants were tested against a potent anti-D serum.

Measurement of Venous Pressure

In some of the earlier cases in this series it was noted that when the cord was cut a few hours after birth, for the purpose of carrying out an exchange transfusion, blood

gushed violently from the vein. In some of the later cases venous pressure was measured as follows:

With the infant supine on a flat surface, a plastic catheter was passed up the umbilical vein for a distance of approximately 2½ in. (6.25 cm.); a little blood was withdrawn and the catheter was then connected to a fine-bored saline manometer. The level of saline in the manometer was raised above the expected venous pressure and allowed to run in slowly until equilibrium was attained and the infant was quiet. The readings were referred to the level of the lower part of the front of the chest, using a wooden rule and spirit level.

Results: A. Haemoglobin Values

Normal Infants

(*a*) *Cord Blood.*—The results of 52 tests on normal infants are plotted in Chart 1; their mean value was 16.35 g.% and their

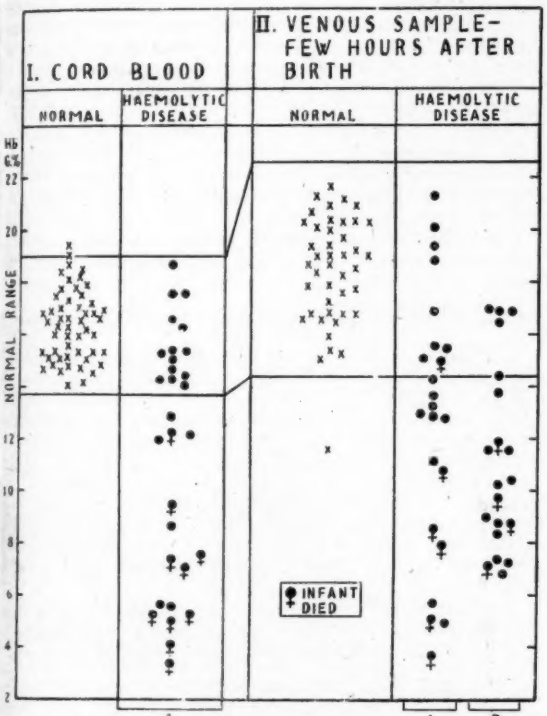

CHART 1.—Hb values in normal infants and in infants with haemolytic disease. I, cord blood; II, venous blood taken a few hours after birth. In II, series "A" are affected infants whose cord Hb is also plotted in I. Series B are infants whose cord Hb was not determined.

S.D. 1.34. The normal range throughout this paper has been expressed as "observed mean ±2 S.D.," which gives a calculated range of 13.7–19 g.%, rather than the observed range of 14–19.4 g.%.

(*b*) *First Day; Venous Blood.*—The mean of 43 observations was 18.45 g.% (S.D. = 2.04); these observations are also plotted in Chart 1. Again the calculated normal range (mean ±2 S.D.) has been considered as the normal range in this paper.

(*c*) *First Day; Capillary Blood.*—The mean value of 33 observations* was 19.1 g.% (S.D. = 1.84).

(*d*) *Changes in Individual Cases.*—In Chart 2 the changes in four selected cases are illustrated. It will be noted that when the cord is tied late the haemoglobin value a few hours after birth is considerably higher than that of cord blood, whereas when it is clamped immediately after birth there is little or no rise in the haemoglobin value. (For detailed observations upon this phenomenon, see De Marsh *et al.*, 1942; these illustrative normal cases are described because they have such a very important bearing on the changes observed in the affected infants.)

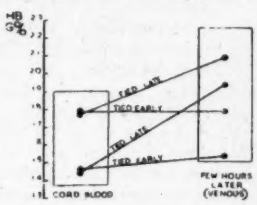

CHART 2.—Four normal infants selected to illustrate the effects of early and late tying of the cord.

(*e*) *Haemoglobin Values After the First Day of Life.*—Only a small group of normal infants was tested at intervals during the first 60 days of life. No infant had a haemoglobin value of less than 11 g.% during this period.

Affected Infants

(*a*) *Cord Blood.*—Thirty infants were tested; 14 had values within the normal range and 16 had values below it, ranging from 3.4 to 12.8 g.%. No deaths occurred among the infants with normal values, whereas there were 10 deaths among the 16 anaemic infants. Moreover, among the 10 infants with cord haemoglobin values below 8 g.% there were only two survivors (see Chart 1).

(*b*) *First Day; Venous Blood.*—Forty-three infants were tested; 14 had values within the normal range and 29 had values below it, varying from 3.7 to 14.3 g.%. These 43 cases included 23 whose cord-blood haemoglobin had been determined. As expected, the first-day values were on the average higher. At the same time the difference was a small one, and this was probably because in many instances the cord had deliberately been clamped as soon after birth as possible.

There were two cases of special interest: two infants whose cord-blood haemoglobin had been 12.3 and 12.8 g.% were found a few hours later to have values of 15 and 15.4 g.% respectively. Thus these two infants had values definitely below the normal range in cord blood, but a few hours after birth, doubtless owing to the fact that they recovered a fair amount of placental blood. they had values within the normal range; that is to say, haemoglobin values no lower than that of a normal infant recovering little or no placental blood.

Of the 20 infants whose cord blood was not tested but from whom a venous sample was taken a few hours after birth four died subsequently; the haemoglobin value of all these four infants was below 12 g.%.

(*c*) *First Day; Capillary Samples.*—In a few infants capillary samples were taken at the same time as venous samples; as in normal infants, the capillary samples gave distinctly higher values.

In Chart 3 are plotted the haemoglobin values observed in one affected and one normal infant. The affected infant is one of the two mentioned above whose cord haemoglobin value was 12.8 g.% and whose first-day venous haemoglobin value was 15.4 g.%; capillary samples taken at the same time as the "first-day venous" sample showed a further rise to 18 g.%. Thus it is clear that a haemoglobin value of 18 g.% in a capillary sample taken from an infant a few hours after birth does not exclude the possibility that a definite anaemia existed at the moment of birth.

The normal infant's cord haemoglobin value was 2.4 g.% higher than that of the affected infant, but because it recovered little placental blood its venous and capillary haemoglobin values a few hours later were no higher than those of the affected infant.

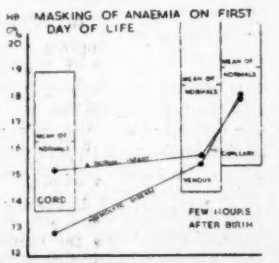

CHART 3.—The Hb value of an infant may rise from 12.9 to 15.4 g.% within a few hours of birth, owing to the transfer of placental blood; on the other hand, the Hb value may change only from 15.2 to 15.8 g.% in an infant who receives a negligible amount of placental blood. The difference between the two infants is thus temporarily masked. Capillary samples usually give considerably higher values than venous samples and thus further mask anaemia.

*This group of observations is not strictly comparable with (*b*). Direct comparisons on the same infants have revealed distinctly greater differences between capillary and venous samples.

(*d*) *Haemoglobin Values After the First Day of Life.*—Seven infants with cord haemoglobin values between 15.1 and 18.7 g.% were left untreated; two other infants seen for the first time during the first three days of life were also judged to be very mildly affected (haemoglobin value within the normal range, mild icterus, weak positive direct Coombs reaction) and were not treated; one further infant was first seen on the 30th day of life and then found to have a moderately strong positive direct Coombs reaction. This infant was known to have shown no trace of jaundice in the neonatal period. The haemoglobin changes during the first two months of life in these ten mildly affected infants are plotted in Chart 4. In addition, an indication is given of the time for which the direct Coombs test remained positive. It is clear that an infant can have a positive direct Coombs reaction for one and even two months after birth without developing any serious degree of anaemia, and can have a positive reaction for two to three weeks without developing any subsequent anaemia at all.

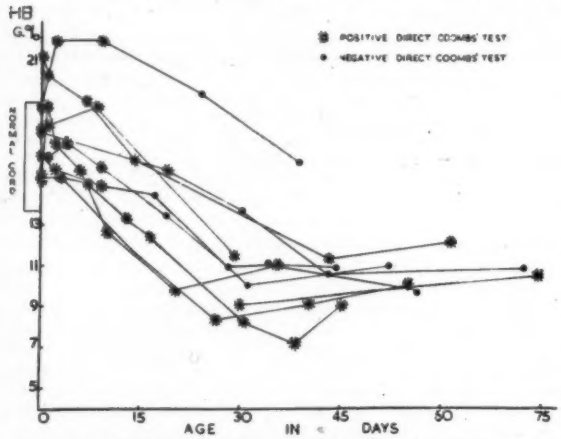

CHART 4.—Hb changes in 10 very mild cases of haemolytic disease. Cord blood: range, 15.1–18.7 g.% (7 cases tested); 30-day venous sample: range 8.2–18 g.% (10 cases tested).

In the cases treated by exchange transfusion the infant was usually provided with a concentration of some 4–5.5 million Rh-negative erythrocytes per c.mm., and this population of cells disappeared at the rate of only 1% a day (with a single exception). Only in two cases in which the infant grew unusually rapidly and in two cases in which the infant was provided with a concentration of less than 3.5 million Rh-negative cells per c.mm. did the haemoglobin concentration subsequently fall to such a level (7 g.%) that it was considered necessary to give a further transfusion. In the remaining infants the haemoglobin fell to 8.5–10 g.% at the end of 30–60 days and then slowly rose spontaneously.

B. Erythroblastaemia

In 49 affected infants a blood film was examined on the first day of life. In 16 cases there were less than 10 nucleated red cells per 100 white cells; in 11 of these 16 the cord haemoglobin had been estimated and in only two was the value below 15 g.% (in these it was 12 and 12.9 g.%). In the remaining five infants, examined a few hours after birth, the haemoglobin varied from 11.6 to 16.9 g.%. All of these 16 infants recovered uneventfully, some without treatment.

In the remaining 33 cases there were at least 20 nucleated red blood cells per 100 white blood cells; in many instances the nucleated red cells far outnumbered the leucocytes and there were numerous primitive forms. Fifteen of these 33 infants died and the remaining 18 all required treatment.

C. Bilirubin Values

Normal Infants.—Cord blood. Twenty-one normal infants were found to have a mean value of 1.6 mg. per 100 ml. with a range of 0.8–2.6 mg.

Affected Infants.—(*a*) Cord Blood:—Thirty-two infants were tested; values ranged from 1 to 9.3 mg. per 100 ml. (see Chart 5). Amongst 11 infants with cord bilirubin values over 4 mg. per 100 ml. there were six deaths. There were only two deaths amongst the 13 infants with bilirubin values between 3 and 4 mg. per 100 ml., and all of the eight remaining infants with values below 3 mg. recovered uneventfully. (*b*) First Few Days of Life:—In the 7 mildly affected infants (referred to above) whose cord haemoglobin lay between 15.1 and 18.7 g.% and who were left untreated, bilirubin values rose from 1–3.2 mg. per 100 ml. in the cord blood to peak values of 1.3–15.8 mg. between the second and fifth days of life.

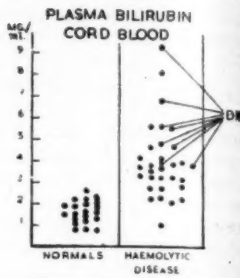

CHART 5.—Cord bilirubin values in 32 affected infants compared with a group of 21 normals.

It is difficult to make useful comparisons between this group of cases and those whose blood had a low haemoglobin value on the first day of life, because the latter infants were treated by exchange transfusion. However, it was striking that in this group the five infants who died at the age of 2–5 days all became profoundly jaundiced despite exchange transfusion, and as early as 24 hours after birth showed bilirubin values between 17 and 21 mg. per 100 ml.

In one infant (which did not develop kernicterus) exchange transfusion was not carried out until it was 12 hours old; during this period the plasma bilirubin rose from 8.1 to 19.3 mg. per 100 ml.

It is obvious that for purposes of comparison it is essential to take cord samples rather than samples a few hours after birth.

Correlation Between Haemoglobin and Plasma Bilirubin Values in Cord Blood

In Chart 6 the haemoglobin and plasma bilirubin values of the cord blood of 24 infants are plotted against one another. It will be noted that there is a correlation between low haemoglobin and high bilirubin values. As expected, the relationship does not appear to be linear. The haemoglobin value doubtless reflects the rate of blood destruction, so that, in general, higher bilirubin values are to be expected when the haemoglobin is low. Nevertheless the amount of bilirubin produced also depends upon the total amount of breaking-down haemoglobin, so that some falling off will be expected when the haemoglobin values are very low. From the Chart it appears that this is the case.

In Chart 6 the infants who died subsequently have been specially marked. It will be noted that there is some suggestion that the bilirubin value and haemoglobin value of a sample of cord blood, when taken together, give a better indication of the prognosis than either value considered separately. A slanting line could be drawn through the observations in such a way as almost completely to separate the living from the dying.

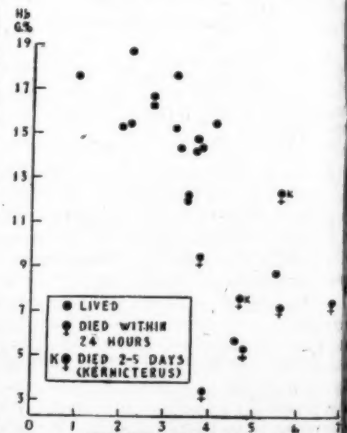

CHART 6.—Cord Hb concentration plotted against cord plasma bilirubin concentration in 24 affected infants.

D. Serological Tests

Direct Coombs Test.—Tests were made on 69 Rh-positive infants born to mothers whose serum contained anti-Rh; all gave positive reactions, though a small number were weak. These weak reactions were shown by infants born to mothers

whose sera contained low-titre albumin antibodies or saline antibodies of low or moderate titre. Further tests were made from time to time during the first three months of life. The results obtained in the untreated cases are shown in Chart 4, and it will be noted that even in mild cases the reaction remained positive for at least 10 days after birth and that in some cases it remained positive for as long as 60 days.

In infants treated by exchange transfusion with Rh-negative blood, Rh-positive cells often disappeared completely within a few days of transfusion or fell to a level of approximately 250,000 cells per c.mm. In these cases the direct Coombs test became negative and did not usually become positive again even when, at the end of 50 or 60 days, there were once more large numbers of Rh-positive cells in the circulation.

In infants treated by simple transfusion of Rh-negative blood there were usually more Rh-positive cells persisting in the circulation, and the direct Coombs reaction remained positive for long periods after transfusion. In one exceptional case the test was still positive 93 days after birth.

Tests for Free Antibody in Infant's Serum.—The sera of 41 infants were examined, either by the indirect Coombs test or by titration in albumin, or by both methods, for the presence of free Rh antibody; one or the other, or both, of the tests was positive in 35 cases.

In 18 cases sera were examined by both tests; in two cases where the infant's serum had a titre of only 2 in albumin the indirect Coombs reaction was negative, and in one case in which the serum gave a weak positive indirect Coombs reaction antibody could not be detected by the albumin test. In the remaining 15 cases the two tests were in agreement.

The amount of free antibody, determined by albumin titration, was not well correlated with the clinical manifestations. For example, amongst eight infants with a titre of 2 or less, three died, four were moderately severely affected, and one was very mildly affected and required no treatment. Among seven infants whose sera had an anti-Rh titre of 16 or more, four died, two were severely affected but recovered, and one was very mildly affected and required no treatment.

Persistence of free antibody does not by itself appear to be associated with tissue damage. In one infant given repeated simple transfusions of Rh-negative blood no Rh-positive cells could be detected between the 14th and the 30th days of life; at the end of this period the infant's plasma still contained Rh antibody to a titre of 32. By the 60th day there were once more many Rh-positive cells present, the direct Coombs reaction was positive again, and there was now only a trace of free antibody. The infant finally recovered completely.

Titre of Rh Antibody in Mother's Serum.—In 62 cases a sample of blood was taken from the mother within 24 hours of delivery. In every case the serum was titrated against CDe/CDe cells both in saline and in albumin. Seventeen of the 62 sera reacted equally well in saline and albumin (i.e., difference no greater than one tube). The remaining 45 sera gave higher titres in albumin; 26 of these gave no reaction at all in saline and nine reacted only in the first tube or the first and second tubes of the saline titration. The remaining 10 sera had titres of between 4 and 32 in saline, but in each case had an albumin titre that was at least four times greater (i.e., more than two tubes higher in the titration).

It is clear that any simple classification of these results must be arbitrary, but it is convenient to consider Rh antibodies in two groups—namely, (1) "predominantly saline agglutinins" (i.e., reacting equally well in saline and albumin): 17 cases; and (2) "predominantly albumin agglutinins" (i.e., titre in albumin two tubes or more higher than titre in saline): 45 cases.

It was noted that amongst the 17 cases in which the mother's serum contained predominantly saline agglutinins there were no stillbirths or deaths within the first 24 hours. However, there were three deaths at the age of 2–5 days, presumably from kernicterus. Amongst the 45 cases in which the mother's serum contained albumin antibodies (predominantly) there were four stillbirths, seven deaths within the first day of life, and four deaths at 2–5 days.

On these figures the difference in total mortality between the group of infants whose mothers' serum contained saline agglutinins (mortality 18%) and the group in which the mothers' serum contained albumin agglutinins (mortality 33%) cannot be considered significant (S.E. of difference = 12.6%). Nevertheless the absence in the "saline group" of stillbirths and deaths within the first 24 hours of life is significant. The milder effects of saline agglutinins are further emphasized by Chart 7, in

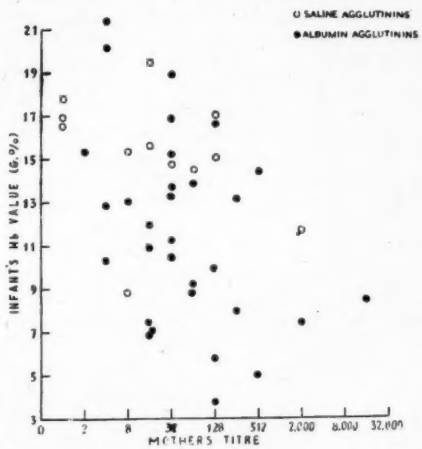

CHART 7.—Titre of Rh antibody in mother's serum (at delivery) plotted against infant's first-day venous Hb value in 43 cases.

which the kind of antibody predominating in the mother's serum, and its titre, have been plotted against the infant's first-day haemoglobin value. It will be noted that in 10 out of the 12 cases in which the mother's serum contained saline agglutinins the infant's haemoglobin value was above 14 g.%.

With regard to sera containing albumin agglutinins predominantly, it appears that there is a correlation, though a poor one, between titre and degree of anaemia. There are few low haemoglobin values occurring with low maternal anti-Rh titres and few normal haemoglobin values occurring with high maternal anti-Rh titres. That this correlation is significant can be shown by dividing the cases into groups having, for example, an albumin titre of 128 or more and 64 or less respectively and showing that there is a significant difference in mortality. When the cases were analysed in this way and stillbirths (not appearing in Chart 7) were included, the results shown in Table II were obtained.

TABLE II.—*Relation Between Titre of Albumin Agglutinins in Mother's Serum and Infant Mortality*

Group	Total	Mother's Titre	Infants		Mortality
			Living	Dying	
I	28	1–64	22	6	21%
II	16	128 and over	5	11	69%

Observed difference between I and II = 48%. S.E. of difference = 14%.

E. Venous Pressure

Venous pressure was measured in 14 infants; in infants without anaemia or with only slight anaemia it was found to vary between +3 and +5 cm. of saline. It is to be noted that this is the pressure below the diaphragm, in the proximal part of the umbilical vein, and represents the pressure above the front of the chest. In infants with severe or moderate anaemia the venous pressure was usually raised, values of +9 to +11 cm. usually being recorded (Table III). In these latter cases the cord often bled violently when cut, and this sign is probably a reliable indication of a raised venous pressure. In a few infants violent bleeding was noticed, although the pressure was not measured, and these cases have also been entered in Table III.

TABLE III.—*Venous Pressure in Cases of Haemolytic Disease*

Name	Haemoglobin		Venous Pressure* (cm. Saline)	Violent Bleeding When Cord Cut	Outcome
	Cord (G. %)	1st Day (G. %)			
Cu. ..	3·4	3·7	+9	+	Died 12 hours†
St. ..	5·3	5·0	+11	+	Died 12 hours†
Ho. ..	—	7·1	+10	?	Died 96 hours†
Wat. ..	5·7	5·7	?	+	Lived†
Ti. ..	—	7·3	?	+	Lived†
O'B. ..	7·4	—	+9	+	Died 13 hours
Th. ..	—	7·4	+7	0	Lived†
Ri. ..	—	8·4	+4	0	Lived†
Ve ..	—	8·8	+5	0	Died 60 hours†
Bl. ..	9·4	10·9	?	+	Died 3 hours†
Du. ..	—	9·8	+3	0	Died 43 hours†
Pl. ..	—	11·9	?	+	Died 24 hours†
Bus. ..	12·2	13·7	+5	0	Lived†
Da. ..	12·3	15·0	+5	0	Died 72 hours†
Sa. ..	12·9	15·4	+4	0	Lived
He. ..	14·7	—	+5	0	Lived†
But. ..	15·4	15·1	+3	0	Lived
Ta. ..	15·4	16·9	+5	0	Lived†

Summary

No. Tested	Haemoglobin (G. %)	Raised V.P. or Bleeding
12	Cord .. 3·4–9·4 1st day .. 3·7–11·9	9
6	Cord .. 12·2–15·4 1st day .. 13·7–16·9	0

* Normal V.P. + 3 to + 5 cm. † Treated by exchange transfusion.

Deaths

Out of 74 cases there were five stillbirths, 10 deaths within the first 24 hours of life, and seven deaths between the second and fifth days of life. There were only two deaths later than this; one infant (Oa.), who was not seen before the third day of life and was treated by simple transfusion of Rh-negative blood, developed signs of kernicterus on the fourth day and eventually died, in a fit, at the age of 4 months; and one infant who recovered from haemolytic disease but developed congenital pyloric stenosis and died after operation. Of the remaining 50 survivors, only one has any signs suggestive of C.N.S. damage.

TABLE IV.—*Analysis of Fatal Cases*

Name	Haemoglobin		Erythro-blastaemia	Age at Death	Mother's Delivery Titre	
	Cord (G. %)	1st Day (G. %) (venous)			Sal.	Alb.
Ant. ..	—	—	Not examined	Stillbirth	—	+
Bu. ..	—	—	" "	"	Nil	260,000
Tu. (2) ..	—	—	" "	"	Nil	2,048
Gr. ..	—	—	" "	"	16	128
Kie. ..	—	—	+ + +	"	Nil	16
Yo. ..	—	—	Not examined	Few mins.	Nil	+
Ca. ..	5·1	—	+ + +	½ hr.	Nil	8
Tu. (1) ..	4·1	8·7	+ + +	9 hrs.	Unknown	
O'N. ..	5·3	—	+ + +	3 hrs.	Nil	128
Cu. ..	3·4	3·7	+ + +	12 hrs.	8	128
St. ..	5·3	5·0	+ + +	12 hrs.	2	512
O'B. ..	7·4	—	+ + +	13 hrs.	Nil	256
Gi. ..	7·1	—	Not examined	11 hrs.	32	256
Ecc. ..	7·6	7·9	+ + +	60 hrs.	Nil	256
Ho. ..	—	7·1	+ + +	96 hrs.	Nil	16
Ve. ..	—	8·8	+ +	60 hrs.	8	8
Bl. ..	9·4	10·9	+ +	3 hrs.	Nil	16
Du. ..	—	9·8	+ + +	43 hrs.	16	128
Pl. ..	—	11·9	+ + +	24 hrs.	4	16
Da. ..	12·3	15·0	+ +	73 hrs.	128	128
Hi. ..	—	14·7 (cap.)	Not examined	96 hrs.	32	64
Wal. ..	—	—	+ +	40 hrs.	Nil	16
Oa.* ..	—	9·1	+	4 mths.	Nil	256

* First examined on third day of life.
+ + + = More than 70 nuc. r.b.c. per 100 w.b.c.
+ + = 30–70 nuc. r.b.c. per 100 w.b.c.
+ = 10–30 nuc. r.b.c. per 100 w.b.c.

In Table IV the time of death is recorded together with the cord haemoglobin and the first-day venous haemoglobin (when known). It is evident that there is a correlation between low initial haemoglobin and death on the first day of life. Moreover, of the seven infants dying between the second and fifth day of life four had haemoglobin values well below the normal range a few hours after birth; one (Hi.) had a value just below the normal range and one (Da.) had a value just within the normal range; however, in this latter infant cord blood had also been tested and found to be anaemic. In the seventh case the haemoglobin value was not determined before transfusion.

Discussion

It has already been mentioned that no infant with a cord haemoglobin value of over 14 g.% died, whereas of 10 infants with values under 8 g.% there were only two survivors. In the intermediate zone there were two deaths among six cases. The idea that the cord haemoglobin is a reliable index of severity receives further support from the observation that seven infants whose cord haemoglobin was within the normal range and who were left untreated pursued a benign course.

Data obtained from the infants first tested some hours after birth lend further support to the theory that initial anaemia is closely correlated with an unfavourable prognosis, since all four deaths in this group occurred in infants whose venous haemoglobin value a few hours after birth was below 12 g.%.

It has long been accepted that infants with hydrops foetalis have a severe anaemia at birth, and it might be suggested that our observations simply restate this fact. It is true that two of the infants whose cord blood was tested were frankly hydropic and others had varying mild degrees of oedema. However, these cases merged imperceptibly into the group who lived on beyond the first 24 hours only to die on the second, third, or fourth days of life; in most of these latter cases it was possible to establish by post-mortem examination that the infant had the changes of kernicterus.

It seems that two distinct mechanisms are operating, and it is to some extent coincidental that the degree of anaemia is correlated with both. It appears that very severe anaemia kills the infant by causing cardiac failure; doubtless the mechanism is similar in many respects to that of the hyperkinetic phase described by Howarth and Sharpey-Schafer (1947) in adults with severe anaemia. The process of birth presumably throws an additional strain on the infant's cardiovascular system and precipitates failure; doubtless also the transfer of placental blood, when it is allowed to occur, may add too great a load.

With regard to the deaths occurring two to five days after birth, two facts seem to be established. First, as Vaughan (1946) and Parsons (1947) have stressed, the deaths are not directly due to anaemia, since many of the infants have haemoglobin values within the normal range at the time of death; it is probable, as Hawksley and Lightwood (1934) first suggested, that the immediate cause of death in these cases is medullary failure consequent upon cerebral damage. On the other hand, these deaths are associated with a certain degree of anaemia at birth, as our observations make clear. The most likely explanation of this association is that the incidence of kernicterus is closely related to the severity of the haemolytic process.

If it is true that the severity of the haemolytic process not only determines the likelihood of the infant's dying from anaemia *in utero* or within 24 hours of birth but also largely determines the possibility of the infant developing kernicterus two to five days later, should it survive so long, other signs of rapid blood destruction besides anaemia should always be present in fatal cases of the disease.

The two most obvious signs to consider are erythroblastaemia and hyperbilirubinaemia. It has often been stated that erythroblastaemia is a variable sign in haemolytic disease, and in the present series of cases it was found in only 33 out of 49 infants examined on the first day of life. However, all of the 16 infants without erythroblastaemia were mildly affected, whereas among the 33 cases

showing erythroblastaemia there were none so mild as not to require treatment. Moreover, these 33 cases included 15 who died within the first five days of life, and in all of these erythroblastaemia was pronounced.

Raised bilirubin values must be interpreted more cautiously, since it is known that the newborn infant has a lowered capacity for excreting bilirubin, and this capacity varies widely from one infant to another; moreover, actual damage to the liver may occur in haemolytic disease (Hawksley and Lightwood, 1934). However, our observation of a moderate correlation between low haemoglobin and high bilirubin values suggests that in fact the hyperbilirubinaemia in infants with haemolytic disease is at least partly due to blood destruction.

The cord bilirubin value, taken alone, does not seem to be quite as satisfactory a criterion of severity as the cord haemoglobin, because only a narrow zone divides mild from severe cases. Not enough data are available to decide whether the haemoglobin and bilirubin values of cord blood, considered together, give a better estimate of severity than either value considered alone, but it is probable that they will prove to do so.

It appears that there is some connexion between the strength of the direct Coombs reaction and the severity of the haemolytic process, since in this series the weakest reactions were found in mildly affected infants. On the other hand, moderately strong reactions were not necessarily associated with signs of rapid blood destruction. One infant who never became jaundiced and developed only a very mild anaemia had a positive direct Coombs reaction for 60 days after birth.

The amount of free antibody in the infant's serum appears to be poorly correlated with severity, since some cases with only traces of free antibody were severely affected and others with moderate amounts of free antibody were mildly affected. At the same time it must be noted that the two infants with the largest amounts of free antibody were both severely affected.

It is evident that there is some correlation between the kind of antibody, and its titre, in the mother's serum and the severity of the disease in the infant, but that the correlation is low, so that exceptions are frequent. In this series the predominance of saline agglutinins over albumin agglutinins in the mother's serum was on the whole associated with milder forms of the disease.

When albumin agglutinins predominated in a serum their titre bore some relation to severity, for there were no very severe cases occurring with very low maternal titres, and deaths were significantly more frequent when the mother's titre was high. Similar conclusions have been reached by Davidsohn and Stern (1948).

Wiener (1946) suggested that the presence of saline agglutinins in the mother's serum caused a disease syndrome "erythroblastosis" associated with deep jaundice and kernicterus; this syndrome was said to come on after birth, since the agglutinins crossed the placenta only during labour and were then thought to cause agglutinative thrombi in the liver and brain; the presence of "blocking" antibodies was said to lead to a different syndrome—"congenital haemolytic disease," associated with anaemia and/or hydrops.

Wiener and Gordon (1948) now consider that saline agglutinins play only a minor part in haemolytic disease, though Wiener (1948) still believes that saline agglutinins may enter the infant's circulation "through placental defects or during labour."

A more convincing hypothesis is that saline agglutinins play no part in the aetiology of haemolytic disease and that sera which contain saline agglutinins can be regarded as containing in addition a smaller amount of albumin agglutinins. This hypothesis would satisfactorily explain the milder effects of saline agglutinins and is also consistent with the evidence that the haemolytic process is already maximal at the moment of birth.

The idea that haemolytic disease "comes on" after birth has arisen from the fact that jaundice and pallor may be absent at birth but develop rapidly afterwards. However, it is well known that the plasma bilirubin rises rapidly after birth in *normal* infants, chiefly because of the poor excretory capacity of the liver in the newborn. Therefore a rapid rise in bilirubin after birth does not indicate that the rate of blood destruction is increasing. Our observations demonstrate that even in very mildly affected infants the plasma bilirubin is usually already raised at the moment of birth, and in severely affected infants is always far above the normal range.

A decline in haemoglobin value during the days following birth is also a phenomenon of all normal infants and has been shown to be due to a diminution in the production of erythrocytes after birth (Faxen, 1937; Shapiro and Bassen, 1941). It is very probable that the rapid fall in haemoglobin values during the first few days of life observed in many infants with haemolytic disease of the newborn is also due to a diminished production of erythrocytes rather than to any increase in the rate of destruction. In one severe case reported by Mollison (1943) the rate of destruction of Rh-positive erythrocytes in an infant with "icterus gravis" was measured on the fourth and seventh days of life and found to be distinctly slower on the second occasion. It is common knowledge that in infants with haemolytic disease the degree of erythroblastaemia diminishes rapidly after birth, and it is surprising that so much stress has been laid on blood destruction as a cause of the anaemia, to the complete exclusion of any consideration of changes in the amount of production.

It has been suggested that there is an inverse relationship between the degree of blood destruction and the development of kernicterus (Vaughan, 1946; Parsons, 1947). It seems to us that this belief has arisen as follows:

Infants whose cord haemoglobin value is below 8 g.% usually die within 24 hours of birth and therefore do not have time to develop kernicterus. Infants with cord haemoglobin values of, say, 10–12 g.% may acquire values of 12–15 g.% in venous samples taken a few hours after birth, and capillary samples may show values as high as 18 g.%. The infant's rapid production of cells does not fall off for two to three days after birth, and therefore an infant whose haemoglobin value was 12 g.% at the moment of birth may die on the third day of life with a haemoglobin value of, say, 16 g.%. The fallacy lies in regarding such a haemoglobin value as being necessarily normal. 16 g.% does lie within the normal range of haemoglobin values for the third day of life, but it is normal only for an infant receiving little or no placental blood. In an infant which has received a large amount of placental blood 16 g.% in a capillary sample taken on the third day of life is indicative of anaemia.

Summary

The haemoglobin value in the cord blood of an infant with haemolytic disease is well correlated with the severity of the disease. Infants whose cord blood contains less than 8 g.% are very likely to die within 24 hours of birth. These infants often show a raised venous pressure and probably die from cardiac failure. Infants with values over 14.5 g.% are very likely to recover without treatment. Deaths from kernicterus at two to five days occur in some of those infants who are anaemic at birth but not so anaemic as to die within 24 hours.

Haemoglobin values of blood samples taken after birth are much more difficult to interpret because of (*a*) the placental

transfer of blood, and (*b*) the large capillary/venous differences in the newborn.

The cord plasma bilirubin taken alone is a less valuable index of severity than the cord haemoglobin. However, taken in conjunction with the cord haemoglobin it is of definite value in assessing the severity.

In this series erythroblastaemia was present on the first day of life in all moderately severe cases and was a striking feature in all the fatal cases; in mild cases the number of nucleated red cells was usually within normal limits.

The strength of the direct Coombs test and the amount of free Rh antibody in the infant's circulation are of very limited value in assessing severity.

The form of Rh antibody predominating in the mother's serum and the antibody titre show some correlation with the severity of the haemolytic process in the infant. In practice exceptions are frequent, and antibody tests can be used only to forecast probabilities.

These findings emphasize the importance of determining the haemoglobin and bilirubin values of cord blood as a means of grading cases of haemolytic disease of the newborn. Not only is this of help in deciding whether treatment is needed, but it should make it possible to compare one treated series with another and to decide whether equal numbers of severe cases have been included.

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The British Council for Rehabilitation, which was founded four years ago, has issued the first number of a quarterly magazine (price 2s.) entitled *Rehabilitation*. It publishes a lecture by Sir Hugh Griffiths surveying the field and describing the aims and methods of rehabilitation. "Rehabilitation *is* treatment," he says, "but it is not the treatment of a disease or an injury but the treatment of the *individual* suffering from the disease or injury"; and Dr. Edward Dunlop, discussing rehabilitation in Canada, makes the point in another way—"Each disabled person has his own rehabilitation problems, varying in extent and character." The journal is intended for medical men and ancillary workers as well as managers of industry and patients. It is obtainable from the British Council for Rehabilitation, 32, Shaftesbury Avenue, London, W.1.

CHEMOPROPHYLAXIS OF EXPERIMENTAL FILARIASIS IN THE COTTON-RAT

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It is well known that the blood-sucking mite *Liponyssus bacoti* is a vector of *Litomosoides carinii*, a filarial parasite of the cotton-rat, and that the infection is used in this country and elsewhere for testing the filaricidal activity of drugs. The earlier investigations were made on wild cotton-rats which were found naturally infected in the field. As caution is necessary in the interpretation of the results of such experiments (Kershaw and Bertram, 1948), the more recent chemotherapeutic trials have been made on infections of known duration artificially induced in the laboratory.

This may be done by exposing rats to infection by placing them for a few days in an artificial rat-nest containing a colony of mites previously maintained on an infected rat. In our experience and that of other workers successful infection of a rat by this method cannot be predicted with any confidence. One of us (D. S. B.), in studies on the role of the mite as a vector, has found that it is much more efficient than was suggested by earlier work. Infection rates of over 80% have been obtained for infective forms in batches of mites, and, although a mite usually contains only a few worms, instances of about 20 or 30, or in one case even 67, infective worms in a single mite have been observed. This range of variation in the number of worms per mite in mites of the same batch tends to be wide and irregular. The selection of a suitable host for the provision of such highly infective mites will be dealt with in a later communication elsewhere. Using batches of these highly infective mites we have been able to eliminate some of the unknown or uncontrollable factors arising from the use of rat-nests by exposing rats to infection by releasing small numbers of the mites (about 20) on each rat for about 24 hours.

In a series of 41 untreated cotton-rats exposed to controlled infection in this way, 35 out of 37 of those rats from which gorged mites were recovered subsequently showed microfilariae in the peripheral blood, but four rats from which no gorged mites were recovered remained negative. Thus about 95% successful infection was obtained provided there was evidence of the mites having gorged on the rat. On the other hand, these results suggest that unless the mites feed freely on the rat infection does not occur.

We have shown elsewhere (Bertram, 1947) that the mites do not transmit all their worms at the first infective blood-meal. Consequently, any estimation of the number of worms transmitted to a rat necessitates dissections of a series of mites before, and of engorged mites after, the transmission meal. Since the number of worms per mite is so variable such estimates are likely to show

considerable deviation from the actual intensity of infection obtained, and in 10 rats for which estimates were made such discrepancies were found to occur. Nevertheless, these dissections are of value since they provide confirmative evidence of transmission having taken place during the act of feeding. Thus in one series the infection rate before the transmission meal was 76%, with a mean of 6.7 worms per mite, and the corresponding figures after the meal were 34% and 1.1 worms.

These observations indicate that, though it is unlikely that the method is suitable for the detection of partial prophylactic action, a drug may be regarded as a complete prophylactic if it prevents the development of infection in a number of animals exposed to infective mites, provided it is known that the infective mites had gorged on the treated animals. With this information at our disposal it has been possible to undertake preliminary experiments to test the prophylactic activity of filaricidal drugs on the following basis.

Basis of the Experiments

Recent work has established the therapeutic efficacy of organic preparations of antimony in filarial infections of man and of cotton-rats. It is not possible to compare the therapeutic activity of the antimonials tested by Culbertson *et al.* (1947a) on cotton-rat infections, but from the experiments on human infections the order of decreasing effectiveness was roughly "neostibosan" (Sb^{+5}), "urea stibamine" (Sb^{+5}), "anthiomaline" (lithium antimonythiomalate) (Sb^{+3}), "solustibosan" (Sb^{+5}), "fouadin" (stibophen) (Sb^{+3}), and tartar emetic (Sb^{+3}).

Of organic preparations of arsenic only the tervalent derivatives appear to have been tested satisfactorily for therapeutic activity. Several of these show pronounced activity—e.g., phenyl arsenoxide, reduced tryparsamide, "halarsol," and neoarsphenamine (Hawking, 1940; Hawking and Sewell, 1948) (microfilariae of *Wuchereria bancrofti in vitro* and adults of *L. carinii in vivo*), the atypical "Melarsen oxide" (*p*-melaminylphenyl arsenoxide) (*W. bancrofti* in man), "mapharside" (Otto and Maren, 1947) (microfilariae of *L. carinii in vitro*), and *p*-arsenosobenzamide dithioglycollate (Otto and Maren, 1947) (adults of *L. carinii* and *D. immitis in vivo*).

A number of metal-free organic preparations of known therapeutic activity in protozoal and bacterial infections —e.g., derivatives of acridine, sulphanilamide, quinoline, and phenanthridine—are relatively or totally inactive as filaricides (Culbertson *et al.*, 1947b; Hawking, 1947), but two new series of metal-free compounds of novel chemotherapeutic type have been recently reported as highly active—namely, (1) cyanine and styryl-dye-type compounds containing a resonating amidinium-ion system (Welch *et al.*, 1947), and (2) derivatives of piperazine, the most active of which is "hetrazan" (1-diethyl-carbamyl-4-methylpiperazine hydrochloride) (Hewitt *et al.*, 1947; Santiago-Stevenson *et al.*, 1947), the most promising filaricide to date. No adequate data appear to be available for the activity or otherwise of suramin (="antrypol"="germanin"="Bayer 205") or of the diamidines.

Compounds which are known to have pronounced prophylactic activity in trypanosome infections are antrypol, a new quinquevalent antimonial drug "MSb" (*p*-melaminylphenyl stibonate), (Friedheim *et al.*, 1947), and, to a less extent, the aromatic diamidines (Fulton, 1944). Antrypol has been shown to owe its prophylactic activity to retention on plasma protein (Dewey and Wormall, 1946), and tissue retention is responsible for the remarkable prophylactic activity of MSb (Friedheim *et al.*, 1947; Rollo *et al.*, in press); a similar mechanism doubtless obtains for the aromatic diamidines. For this reason, and since a number of quinquevalent antimonials have been shown to exert filaricidal activity, the three compounds chosen for preliminary prophylactic tests on *L. carinii* infections of cotton-rats were (*a*) antrypol, (*b*) stilbamidine, and (*c*) MSb.

Results

The trial of these three drugs was undertaken by administering a single dose in solution into the peritoneal cavity and allowing the condition of the survivors to become stable. The rats were then exposed to the bites of about 20 highly infected mites, and estimations of the probability of their developing an overt infection were made by recording the number of gorged mites recovered and by dissections of samples of the mites before feeding and after recovery. Five groups of eight rats were exposed to mites, each group consisting of two controls which had not received any drugs and three pairs to which had been given MSb, stilbamidine, and antrypol.

The successful transmission of infection can be established by the appearance of microfilariae in the peripheral circulation about 50 days after the exposure to infective mites or by the examination of the animal some two or three months after exposure to determine whether adults have been produced, for it is possible in low-grade infections in which one or two adults have developed to maturity for one sex only to be present and for microfilariae thus to be absent. In this preliminary trial it was decided to allow the infections which might develop to run their natural course in the first three groups, as it was possible for infection to be delayed in appearance if not prevented, for its subsequent evolution to be protracted, or for its intensity to reach a lower level than those in the controls. The results are shown in the following table.

Chemotherapy of Experimental Filariasis

Drug	No. of Rats	Dose (mg./kg.)	Prophylactic Interval (Days)	Infection Developed
None	10	—	—	1—* 9+
MSb	1	1,000	3	D†
	1		2	—
	1		4	+‡
	1		6–23	‡
	1	500	3	—
	1		6–23	—
	1		7–24	—
	1	250	7	—
	1		21	—
	1		21	—
Stilbamidine	1	50	2	D†
	1		2	+
	1		3	D†
	1		3	+
	1		3	+
	1		4	+
	1		4	+
	1		17	+
	1		17	+
	1	25	4	+
Antrypol	1	500	3	D†
	1		4	D†
	1		4	+
	1		6	D†
	1		6	+
	1		7	—§
	1		7	+‖
	1		21	—*
	1		21	—*
	1	250	4	+

* Not expected to develop an infection, as no gorged mites were recovered.
† Died after exposure to mites.
‡ Developed an infection of low intensity. The antimony content of the blood as determined by trypanocidal titre *in vitro* was between that of a control and another animal which had received a smaller dose of drug. It is presumed that some of the drug had escaped into the gut or had been excreted.
§ Failed to develop an infection (infection probability 95% in control rats).
‖ Died three weeks later from heat-stroke. Five adult females and one adult male were found.

The rats to which MSb had been given were examined at intervals varying from four months to nine months after exposure to determine whether adults might be present

in the absence of microfilariae in the peripheral circulation, but none was found.

It is evident that after a single dose MSb can act as a prophylactic against the development of filariasis in the cotton-rat by preventing the establishment of adults in the pleural cavity after the exposure of the animal to the infective larval form in the mite, so far as these experiments show, at a minimum dose of 250 mg. per kg. of body weight and with a maximum prophylactic interval of three weeks. Stilbamidine and antrypol are both inactive at doses of 50 mg. and 500 mg. per kg. respectively at shorter intervals.

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INFECTED INTERVERTEBRAL DISK AFTER LUMBAR PUNCTURE

BY

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AND

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The use of lumbar puncture as a diagnostic and therapeutic measure is so common that any complication which results from it merits attention. In a review of the literature we found reports of 44 cases of injuries to intervertebral disks, clinically and radiologically established, following lumbar puncture. Only two of these, however, were complicated by infection of the disk or adjoining vertebral bodies.

The majority of cases occurred in children on whom lumbar puncture had been performed for meningitis; those in adults followed a spinal analgesic or some procedure such as encephalography. One of the two infective lesions reported, that by Findlay and Kemp (1943), describes osteomyelitis of the second and third lumbar vertebrae, with destruction of the intervening disk, in a 1-month-old child following an unsuccessful attempt at lumbar puncture in the presence of pyogenic skin infection. The second case (James, 1946), that of a 4½-year-old boy, has some features in common with our own. One week after a difficult lumbar puncture he developed a temperature of 104° F. (40° C.) and flattening and rigidity of the lumbar spine. Shortly afterwards a radiograph showed loss of L3–L4 disk space and later of L4–L5 space with sclerosis of the adjoining vertebral bodies. The illness was complicated by the development of chicken-pox, but recovery followed plaster immobilization and penicillin therapy.

The clinical picture in all the reported cases—whether accompanied by infection or not—is remarkably constant. At a varying interval after lumbar puncture low backache occurs, accompanied by rigidity of the lumbar spine and diminution of the normal lumbar lordosis. Radiological examination subsequently reveals some loss of intervertebral joint space and, later, sclerosis of the adjacent cortex of the related vertebral bodies. Frequently lumbar puncture has either been repeated or been accomplished with difficulty.

In addition to the two infective complications already quoted, one case of spinal epidural abscess after lumbar puncture had been reported up to the end of 1945 (Rangell and Glassman, 1945).

Case Report

A girl had an attack of meningococcal meningitis in 1943, at the age of 12 years, for which she was treated first at a fever hospital and then at a general hospital elsewhere. Exact details are not known, but she remembers that at least one lumbar puncture was performed under an analgesic. She made a good recovery from her meningitis, but experienced backache and severe stiffness during convalescence. The backache has been present on and off ever since; it has never been severe, nor has it radiated from the lumbar region.

Two years after her illness she developed a tender mass above the middle of her left groin and was treated by sulphonamides and local heat. The mass persisted and she became ill, being admitted to hospital with an irregular pyrexia. A provisional diagnosis of actinomycosis was made at this time and she was given 5,500,000 units of penicillin. The mass softened centrally and discharged pus, from which, however, no streptothrix filaments were isolated. After a further course of 7,500,000 units of penicillin the skin over the sinus healed and she was discharged in good general condition.

In October, 1947, she was admitted to St. Mary's Hospital for the first time with a recurrence of the swelling above the left groin. There had been no exacerbation or alteration in the intensity or character of her backache. A radiograph of the pelvis showed no abnormality. Examination under an anaesthetic revealed no palpable intra-abdominal mass. The swelling was subsequently explored and a specimen of tissue sent for histological examination. This revealed chronic inflammatory changes only, and showed that the deep part had not been completely excised. The wound healed, however, and the patient was discharged.

She was readmitted in January, 1948, because a sinus had formed at the site of the operation. Culture yielded *Staphylococcus aureus*. Lipiodol injection and *x*-ray examination of the sinus showed a track 16 cm. long going across the midline to just above the right anterior-superior iliac spine. A lateral radiograph revealed that the sinus lay in the anterior abdominal wall. No connexion with bone or viscus could be demonstrated.

It was decided to explore the sinus track, and this was done by Mr. A. E. Porritt on Feb. 11. The track lay in its proximal 8 cm. entirely superficial to the aponeurosis and, immediately to the right of the midline, passed deeply, lying on the anterior aspect of the rectus muscle and then between the aponeurosis of the external and internal oblique muscles. It was traced to just above the anterior-superior spine, where no further extension could be found. The wound was then closed, and it healed by first intention.

Further radiological examination was carried out by Dr. T. Richard Riley, who reported on the lumbar spine as follows (see Fig.):

"There is a mild scoliosis convex to the right. The body of L3 shows evidence of irregular bone destruction on its lower surface. The affected margins are sclerosed and there is no sign of present activity. The upper surface of the body of L4 shows irregular shallow bone destruction and appearances otherwise as in L3. The intervertebral disk space between L3 and L4 is still present, but considerably reduced in depth. *Comment*:

The appearance of the contiguous surfaces of the bodies of L3 and L4 and that of the intervening disk space is consistent with an old localized infective process at this level. The appearance is not that of tuberculous infection. The retention of some degree of disk space, the absence of paravertebral shadow, and the limited involvement of the upper surface of the body of L4 are not consistent with tuberculous destruction. I would say that the appearances are consistent with a pyogenic infection secondary to lumbar puncture."

Radiograph showing antero-posterior view of lumbar spine.

The patient was put into a plaster jacket and discharged in good condition on March 1. When seen in May, 1948, she was in excellent health and had been comfortable and free from backache in her jacket. The operation wound had remained healed and there was no evidence of any recurrence of the abscess. Her E.S.R. at this time was 3 mm. per hour (Westergren). She was fitted with a lumbar support to be worn in the daytime only.

Discussion

The manner in which the infection in this case presented is interesting. No doubt intensive sulphonamide and penicillin therapy altered the course of the infection, but this cannot explain how an L3–L4 intervertebral abscess tracking laterally round the right side of the abdominal wall should present itself in the left mid-lateral line 5 cm. above the inguinal ligament. At first thought it is tempting to postulate that the pus followed the course of the anterior primary ramus of a lumbar nerve or of a lumbar branch of the abdominal aorta, but simple anatomical considerations show this to be unlikely.

In the majority of reported cases, as in this one, there was no history of sciatic or other root pain, or any related deep segmental pain, in spite of the obvious intervertebral joint disorder. A more detailed study of these patients may throw some added light on the mechanism of pain in intervertebral disk injuries.

The fact that the majority of reported cases have been in children could be accounted for because of the greater frequency of meningitis in children. It is, however, likely that, overall, at least as many lumbar punctures are performed on adults as on children, and the relative frequency of complications among children is therefore probably significant. The danger of intervertebral disk damage is clearly related to the fact that in children the depth of the disk from the skin is much less than in adults, which therefore allows for a smaller margin of error. The annulus fibrosus in young children is no more than 2–3 mm. in depth, and is considerably stretched and thinned in acute flexion of the spine, the standard position for lumbar puncture. Further, the nucleus pulposus is known to be under considerable tension, bulging backwards in acute flexion, and this makes for its easy escape along the needle puncture or its infection by the same means.

Consideration of all these factors might help to minimize the danger of intervertebral disk damage following lumbar puncture, particularly in children.

We are indebted to Mr. A. E. Porritt, under whose care this patient was admitted, for permission to publish this report, and to Mr. V. H. Ellis for helpful advice.

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COUGH FRACTURE OF RIBS

BY

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The purpose of this paper is to call attention to an infrequent but possibly often unrecognized cause of pain in the chest of sudden onset and resembling dry pleurisy in its symptoms. I have observed a number of cases of "spontaneous" fracture of ribs occurring in tuberculous subjects, in some of which there was a clear history of pain following violent expiratory effort as in coughing or sneezing. These cases happen to have been discovered in women aged between 18 and 35, but other authors have recorded it occasionally also in men.

This condition, which I will describe as cough fracture of ribs, is not widely recognized, and the literature on the subject is scanty.

Halliwell (1929) reported fracture of the sixth, seventh, and eighth ribs after a bout of coughing in a doctor aged 40, of good physique and convalescent from pleurisy and "pseudo-asthma." About a month later, on getting out of a bus, he had another attack of coughing, and *x*-ray examination revealed a fracture of the ninth rib on the same side as before and in line with the other three. Recovery was uneventful. Howson (1934) was able to trace, in all, 58 reported cases, and added a further case of his own. This occurred in a woman of 26 with bilateral pulmonary tuberculosis who had had a thoracoplasty on the left side, and several months later was found to have a recent fracture of the ninth right rib, older fractures of the tenth and eleventh right ribs, and a fracture of the left tenth rib "with considerable callus formation." Sakka (1938) also described three cases of spontaneous rib fracture occurring in North African natives which he thought were due to tuberculous osteitis. The subjects were all men between 24 and 27, two of whom were suffering from pulmonary tuberculosis. Cramer (1943) described four cases —three in women aged 26, 65, and 72, and one in a man of 72. He thought the fractures were due to muscular action on areas of rarefaction in the ribs, and suggested that the upper five ribs are unlikely to fracture from cough because they are shorter and are supported posteriorly by the scapular musculature.

Case Reports

Case 1.—A woman aged 23 was admitted to Black Notley Hospital on April 8, 1937, for tuberculosis of the left lower lobe. *X*-ray examination on admission revealed, in addition to the tuberculous disease, a recent fracture of the seventh left rib about 1½ in. (3.75 cm.) from its junction with the costal

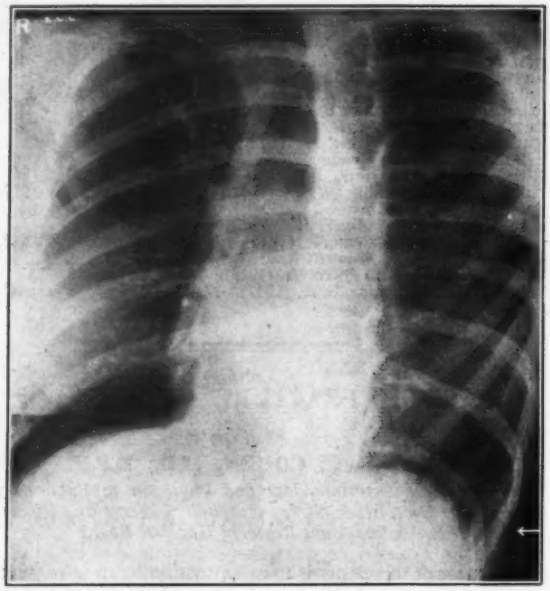

FIG. 1.—Case 2. Dec. 30, 1937. Oblique film. Fibrocaseous tuberculosis of right upper lobe; recent fracture tenth left rib.

cartilage. The patient gave no history of trauma or sudden pain, but confessed to having had some pain in that area shortly before admission. She had had cough and sputum for about three months.

Case 2.—A woman aged 28 was admitted on Oct. 14, 1937, for sluggishly active tuberculous disease of her right sub-apex with a small cavity. On Dec. 30 she complained of soreness in her left side, which she first felt during a bout of coughing. Physical examination revealed a small bump palpable on the angle of the tenth rib, and *x*-ray examination revealed a fractured rib in that position (Fig. 1). Subsequent films showed callus formation which had almost completely absorbed by June, 1938.

Case 3.—A woman aged 22 was admitted on Feb. 18, 1938, for fibrocaseous tuberculosis of her right upper lobe with cavitation. A radiograph on admission showed recent fractures of the anterior ends of her seventh and eighth left ribs, 1¼ in. from the costo-chondral junctions. She had not complained of pain at that site, and there was no history of trauma.

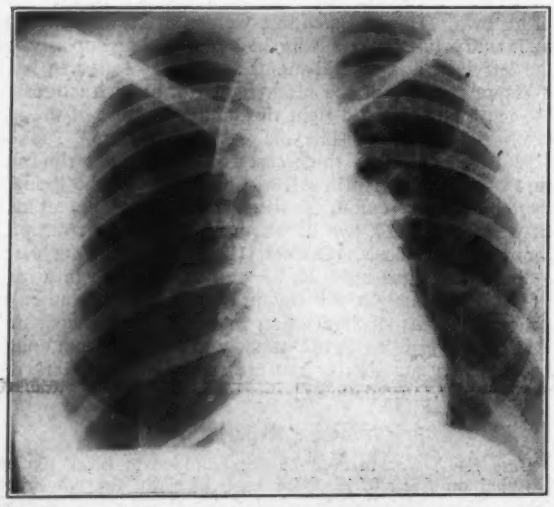

FIG. 2.—Case 4. Sept. 26, 1941. Right artificial pneumothorax, with small effusion; fracture with callus formation.

Case 4.—A woman aged 18 was admitted on April 26, 1938, with acute exudative tuberculosis of the right lung with cavitation. Right artificial pneumothorax was induced on May 2 and adhesions were cut on Nov. 9. She was discharged quiescent on May 7, 1939, and thence attended as an out-patient for refills. A routine *x*-ray examination on Sept. 26, 1941, showed a fracture of the seventh right rib about 2 in. (5 cm.) from the corresponding transverse process, with some callus formation (Fig. 2). The patient gave no history of pain or trauma.

Case 5.—This patient, aged 19, was admitted on Dec. 1, 1939, for exudative tuberculosis with cavitation of her right middle and lower lobes. A radiograph on Dec. 5 showed a fracture with early callus formation of the anterior end of her ninth right rib, about 1 in. (2.5 cm.) from the costo-chondral junction. There were no symptoms at the time of discovery, but on inquiry the patient recalled an acute pain which she had felt low down in her right chest, after a sneeze, a few days before admission.

Case 6.—A woman aged 33 was admitted on March 8, 1948, for fibrocaseous tuberculosis of the left lung with upper-lobe cavitation. A radiograph showed old nearly healed fractures of the fifth, sixth, and seventh ribs on the right side, about 4, 3½, and 3 in. (10, 8.75, and 7.5 cm.) respectively from the

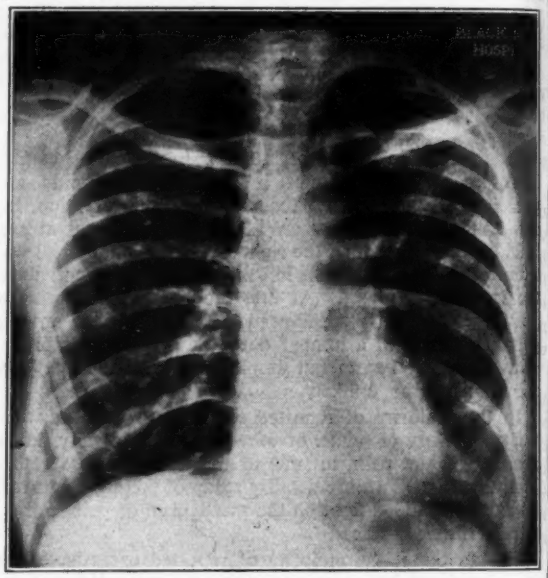

FIG. 3.—Case 6. April 6, 1948. Bilateral tuberculosis of acute exudative type, with cavitation left apex and right sub-apex; fractures with callus formation of fifth, sixth, and seventh right ribs.

costo-chondral junction, so that the fractures appeared vertically above each other (Fig. 3). In November, 1947, she had felt a sudden pain in the right side of her chest, much worse on coughing and catching her breath. She found relief by pressing her hand to her side. The pain lasted about two weeks, gradually diminishing.

Case 7.—A woman aged 35 was transferred to Black Notley Hospital from another sanatorium on March 31, 1948, for fibrotic tuberculosis of her left lung. A radiograph on April 2 showed a fracture of the anterior end of her sixth left rib, 1 in. from the costo-chondral junction. Reference to her previous radiographs showed that the fracture first appeared on an *x*-ray film dated Feb. 13, 1948—it was not seen on the preceding film of Dec. 3, 1947. About Dec. 20 she had felt a sudden pain in the lower part of her left chest which "caught her breath" and was diagnosed as pleurisy. Her chest was strapped for seven days and the pain eased off after a day or two. There was no history of trauma, and she did not think the pain followed coughing, but could not remember for certain.

Discussion

These cases, together with those already reported by other writers, show clearly that it is possible for ribs to fracture as a result of otherwise normal respiratory exercise. The occurrence must be a rare one, but is likely to be observed occasionally by those who see a sufficient number of chest radiographs, and it probably occurs more often than might be supposed. Cases are easily missed if chest radiographs are not carefully examined and the condition borne in mind.

The mechanism of such fractures is difficult to determine. Primary tuberculous osteitis of ribs is generally believed to be so uncommon that it is unlikely to be the basic cause. There was no evidence of it in my own cases, though it is conceivable that areas of bone rarefaction may occur in a rib adjacent to a cold abscess arising from a caseous tuberculous gland; and, so far as I have been able to ascertain, most reported cases, excluding those due to gross localized changes such as secondary malignant deposits or osteitis fibrosa, have occurred in tuberculous subjects, but the condition is not confined to them. Cough fractures of ribs have also been known to occur in elderly subjects, probably associated with increased fragility of bones associated with advancing age, and it would not be surprising if it occurred also, for example, in cases of rheumatoid arthritis, in which rarefaction of bones is sometimes found.

The apparently high incidence in tuberculous subjects suggests a possible constitutional effect on bone structure, but it must also be remembered that such subjects are repeatedly having their chests *x*-rayed and the lesion is therefore more likely to be discovered.

I have been unable to find any evidence to suggest that the ribs of a tuberculous patient are particularly liable to decalcification, except in so far that prolonged bed-rest may lead to some degree of this from diminished use. Certainly the blood calcium level remains remarkably constant in tuberculous subjects. Healing of the fractures has followed normally, and there does not appear to be any delay in callus formation and eventual union.

The most reasonable explanation of these fractures seems to be the violent and abnormal action, probably associated with asymmetrical posture producing uneven action on the ribs, occurring during the violent expiratory effort of a cough or sneeze. Diminished use of the thoracic musculature that occurs in a patient confined to bed for long periods may also lead to a mild degree of decalcification and be a contributory factor.

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The Mental Survey Committee of the Scottish Council for Research in Education has recently completed an investigation into the intelligence of Scottish children. The results were briefly described in *The Times* of Nov. 17, 1948, by Professor Godfrey Thomson, the chairman of the committee. The full results are to be published in a series of volumes, the first of which will appear in the spring. The main task of the investigators was to repeat a group intelligence test given in 1932 to 87,498 Scottish children whose eleventh birthday fell in that year. The same test was given to 70,805 children whose eleventh birthday fell in 1947, but on this occasion much additional sociological information was collected about each child. The possible score was 76 points, and in 1947 the mean score, 36.7, was higher than the mean score, 34.5, in 1932. The boys went up 1.3 and the girls no less than 3.2 points. At least as a first deduction this appears to show that no decline in intelligence is going on, but Professor Thomson thinks the rise may be due to the fact that children are now much more familiar with intelligence tests. The now common observation that intelligent children are more frequently found in small families than in large ones is confirmed. The average score obtained by the only children, 7,824 out of 70,805, was 42 points, and children of families of two averaged nearly as much. But for families of four the average score was 35.3 and for those of eight 28.8.

COUGH FRACTURE IN LATE PREGNANCY

BY

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Rib fractures due to cough alone, or with an added factor of shearing stress from simultaneous action of other muscles, have been recognized for many years (Gurlt, 1862; Tunis, 1890; Hawley, 1890; Skyrme, 1890; Bähr, 1894). In addition, sneezing, choking, vomiting, and straining at stool are recorded as causes among other varieties of expiratory effort. Numerous forms of exertion, such as a handspring or mounting a restive horse (Hilton, 1852; Seilin, 1917), have also been blamed, although here again associated grunting expiration through partly closed cords may have been responsible.

In recent years the number of cough fractures reported from sanatoria has tended to overshadow the non-tuberculous cases, which may be more numerous but have less chance of being diagnosed. Oechsli in 1936 found 77 cases of cough fracture in the literature to that time. He indicated that when a routine search was made in chest films the incidence of the condition was high. In his series of approximately 3,000 admissions to Olive View Sanatorium 22 cases with cough fracture were found. At the same time Richardson (1936) at Ray Brook Sanatorium reported 20 cases out of 1,903 tuberculous admissions. Osteoporosis in the late stage of phthisis has often been suspected as predisposing to cough fracture, but evidence that it is the chief cause is as yet unconvincing.

Tunis (1890), analysing 40 such stress injuries from muscular action, noted that more than 25% occurred in patients in whom bone fragility could be excluded as a factor, and Seilin (1917) supported this view. Reports since published do not suggest a different conclusion.

Kleiner (1924), quoting Tunis and bringing the literature up to date, found that of 57 cases (which included 14 by muscular action other than coughing) 28 were left-sided, 17 were right-sided, and the side was unrecorded in the remaining 12. There were more fractures of lower ribs than upper, the site of fracture on 19 occasions being the upper seven ribs and on 36 occasions the eighth, ninth, tenth, and eleventh ribs. (The apparent discrepancy is due to more than one rib being involved in some instances.) Kleiner's analysis was made before the papers on the large series of tuberculous cases had been published. In seven of eight patients with fracture of the eleventh rib reported by Tunis and Seilin this was the only rib affected. Multiple fractures appear to be more frequent when the higher ribs are involved.

The older writers (Tunis, 1890; Bähr, 1894) suggest that the preponderance of left-sided damage pointed to a cushioning action of the liver on the right side. Oechsli found no left-sided prevalence and was therefore sceptical of this theory, but the majority of his fractures were mid-thoracic and above liver level. Richardson in a similar series of tuberculous patients noted that the sixth and seventh ribs in the mid-axilla were the commonest sites.

In the literature there are six reports of this accident in pregnancy. Only one occurred during labour, and that in

a coughing fit (Ahern, 1894). Wahl (1926) remarked on the coincidence that four out of five cases described had occurred at the end of pregnancy; the duration of cyesis in the other was not recorded. These cases reported by different authors over many years, together with the four patients in the present series, appear to have features in common: (1) they occur late in pregnancy; (2) they tend to be left-sided; (3) lower ribs are chiefly involved; and (4) multiple fractures are the exception. The details are summarized for convenience in the Table.

Author	Patients' Age and Previous Pregnancies	Duration of Pregnancy	Site of Rib Fracture	Remarks
Hérard (1855) ..	22	7 months	Left 11th	Cough for 6 months
Benoit (Bähr, 1894)	—	In 9th month	Left 9th	Coughing fit (ch. bronchitis)
Chonery (Bähr, 1894)	23	—	—	Coughing fit
Dogadkin (1885) ..	27 multipara	In 9th month	Left 8th	" "
Blanc (1908) ..	—	At end of pregnancy	Multiple	Coughing
Ahern (1894) ..	—	In labour	Left 6th	Coughing fit
Paulley *et al.* ..	21 primipara	36 weeks	Left 10th	Coughing fit (ch. bronchitis)
" " ..	25 multipara	38 "	Left 9th and 10th	Coughing mildly
" " ..	36 "	40 "	Left 11th	Lifting and coughing
" " ..	25 primipara	29 "	Left 11th	Coughing after previous choking

Case Reports

Case 1.—Primipara aged 21. 36 weeks. No previous fractures. When seen on Jan. 12, 1947, gave a history for 14 days of sharp pain in the lower left chest posteriorly. A non-productive barking cough had been present for the same length

FIG. 1

of time. Physical signs suggested a small effusion at the left base and chronic bronchitis. *X*-ray film of chest was negative. Subsequent examination revealed a localized tender lump with crepitation over the tenth rib on the left side. Special views of this area confirmed diagnosis of rib fracture. Control films for bone density showed no osteoporosis. Serum calcium was 9.5 mg. per 100 ml. Serum inorganic phosphate was 3.8 mg. per 100 ml.

Case 2.—Multipara (one previous child) aged 25. 38 weeks. No previous fractures. Seen in antenatal clinic on Jan 7, 1948. In late November, 1947, began to cough and noted slight pain in left lower chest. In mid-December, 1947, three weeks before being seen, while coughing mildly felt a crack

FIG. 2

in same region, with exacerbation of pain. Pain had persisted. On examination, tender over left tenth rib in the posterior axillary line. Radiograph of this area confirmed fracture of this rib and of the ninth. Control films for bone density showed no osteoporosis. Serum calcium was 10.3 mg. per 100 ml. Serum inorganic phosphate was 4.6 mg. per 100 ml.

Case 3.—Multipara (four previous pregnancies, well spaced) aged 36. 40 weeks. Seen Feb. 14, 1948. Gave history of having had a cough for some time. Seven days previously coughing vigorously, and at the same time, when bending and lifting a child aged 3, experienced a sudden pain in the left side of chest and felt something "go." Thereafter unable to cough properly because of pain. Clinically, fracture of eleventh rib left side posterior axillary line with ecchymosis. A.P. radiograph of area confirmed fracture. Comparative control radiographs for decalcification revealed no abnormality. Serum calcium was 8.9 mg. per 100 ml. Serum inorganic phosphate was 4.5 mg. per 100 ml.

Case 4.—Primipara aged 25. 29 weeks. No previous fractures. Seen on Jan. 26, 1948, having had cough for three or four weeks. In early January had had a choking attack and subsequently noticed pain over the left lower chest. Two days before attending had gone out in the evening, and cold air in the street caused her to cough, which was followed by immediate sharp pain in the left side. Radiograph confirmed fracture of eleventh rib. Radiographs for bone density against control revealed slight osteoporosis present. Serum calcium was 10.8 mg. per 100 ml. Serum inorganic phosphate was 4.07 mg. per 100 ml.

A woman in late pregnancy was seen in April, 1946, with what was in retrospect a characteristic history. At the time pleurisy was suspected. A radiograph of the chest was negative and she was dismissed as having had an intercostal muscle tear. It is noteworthy that in her case the lesion was on the right side.

Two other probable cases have been seen, but the considerable administrative difficulties in the immediate antenatal and post-natal periods interfered with the necessary investigations.

The Clinical Picture

If the possibility of the condition is kept in mind a careful history will often give a pointer to the diagnosis. The sudden onset of severe sharp pain during a coughing fit is often supported by a story of something "giving" or "cracking." The four cases described, and the other three possibles, all occurred in the first quarter of the year, when hard unproductive coughs are prevalent and bronchitics are having their winter exacerbations. All the patients were in the last three months of pregnancy.

On examination there may or may not be some fever from the primary chest condition, and the respiration rate may be raised owing to pain on deep breathing. Movement and air entry are diminished at the affected base, and percussion is impaired because of poor aeration or a high diaphragm. Pleural rubs have been noted in some cases of cough fracture. The signs may suggest a small pleural effusion, but it must be stressed that postero-anterior and lateral chest films reveal no abnormality when the lower ribs are involved. If suspicion has not already been aroused it is now that a careful search should be made for a tender localized area on one or more of the ribs. Experience of these pregnancy cases suggests that the left ninth, tenth, or eleventh ribs are the most likely site. Antero-posterior and oblique views will be required to confirm a fracture with minimal displacement in or behind the posterior axillary line.

Discussion

Comparisons of bone density against controls of the same sex and age revealed slight osteoporosis in only one case. Blood calcium and phosphorus estimations were within normal limits. There was no history in any of the cases of previous fractures to suggest pre-existing bone fragility.

If calcium or phosphorus metabolism were a factor in late pregnancy patients one might expect a high incidence in the early puerperium, but so far there is no record of such a case.

If bone fragility can be excluded the remarkable incidence of fracture of lower ribs consistently left-sided and in late pregnancy could be due to a mechanical cause peculiar to the abdominal mass or compensatory lordosis.

It has already been shown that the mid-thoracic fractures occur along the line of interdigitation of the external oblique and serratus anterior (Oechsli, 1936), and are assumed to be the result of shearing stress. The likelihood of fracture is reported to be increased if the serratus is taut at the time of coughing, as it may be when the arm is raised or when the patient is resting on one elbow (Atkinson, 1898 ; Seilin, 1917 ; Oechsli, 1936).

In the group of cases in which fracture occurs in the lower ribs a different explanation must be sought. Expiration, normally passive, becomes forced on coughing, but there is some disagreement about which muscles are implicated. Mainland (1945) gives these accessory muscles as: (1) anterior abdominal muscles ; (2) latissimus dorsi, but states that its mechanism is not clear ; (3) the long back muscles, the lower parts of which are able to depress the ribs.

A study of the anatomy and fracture sites in the majority of pregnancy cases suggests that the shearing stress occurs along the line between the origin of the external oblique (from the lower four ribs) and the costal slips of the latissimus dorsi. This, however, ignores the long back muscles (sacrospinalis). In the pregnant stance the head and shoulders are thrown back ; compensatory to this is a lordosis involving increased postural tone, and perhaps hypertrophy of the iliocostalis and longissimus portions of the sacrospinalis. Incoordination or action of more than normal violence might occur in this muscle in such circumstances. Thus forcible expiration, as in coughing with depression of the lower ribs by the iliocostalis, could provide conditions for a shearing stress sufficient to fracture a rib.

Another possible mechanism is that the uterine mass is driven backwards and upwards against the inner surface of the lower chest in coughing by contraction of the anterior abdominal muscles. The main force would be deflected to the left side by the liver on the right. Whether or not the protuberant abdomen is in any way responsible by altering the action or direction of pull of the external oblique must remain at present a matter for further consideration.

Although a fractured rib is a trivial injury it can produce extreme discomfort and insomnia, particularly in a patient who is coughing. That this is undesirable in late pregnancy is self-evident. It would appear from the literature quoted in this paper, and from the present series collected without propaganda in twelve months from two antenatal clinics, that the condition in late pregnancy is not a rarity, and its frequency is probably greater than hitherto appreciated.

The importance of wider recognition lies in the great relief of pain experienced by the patient with early diagnosis and adequate strapping of the chest. Almost equally important is the avoidance of tiresome confinement to bed and needless investigation, often in hospital.

Summary

A brief review of the literature of cough fracture is given, with particular reference to its incidence in late pregnancy.

The clinical picture usually found in this condition is described.

Brief histories of four cases are reported.

Suggestions are made about the mechanism of the condition.

A case is put forward for this rather trivial injury to be regarded more seriously, and a suggestion is made that its frequency may be greater than is generally recognized.

We wish to thank Drs. J. N. Pattinson, F. Pygott, and R. A. H. Kinch for their help, and Miss W. P. Cory and Miss D. Wrighton for secretarial assistance. We are grateful to Mr. J. S. MacVine for access to three of the cases, to Mr. F. Roques for access to the fourth case, and to Professor J. Kirk and Dr. E. W. Walls for advice on the anatomy.

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LYMPHOBLASTIC LEUKAEMIA TREATED WITH URETHANE

BY

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The use of urethane in the treatment of lymphatic leukaemia is a fairly recent development, and was first recorded by Paterson *et al.* (1946) in 12 cases of chronic lymphatic leukaemia. Five of these patients were alive at the end of the observation period, but the single case of acute lymphoblastic leukaemia showed no response to treatment.

The following case is noteworthy for the dramatic initial clinical and haematological response to urethane in a child with acute lymphoblastic leukaemia.

Case History

A girl aged 14 months, weighing 24 lb. (10.89 kg.), was admitted to hospital on July 19, 1947, with one week's history of anorexia and fretfulness, associated with vomiting for the previous two days. The mother had recently noticed that the child bruised easily. The past history was one of normal physical and mental development, the diet was normal, and no drugs had been taken. The family history was negative.

On examination the patient was seen to be a well-developed but abnormally quiet child with a very pale, slightly jaundiced skin. Small ecchymoses were present on the limbs, though petechiae were not seen. There was uniform enlargement of the cervical glands, and those of the axillae and groins were easily palpable. The spleen was enlarged to three finger-breadths below the left costal margin and was soft in consistency. The liver could not be felt ; the mucous membranes showed neither haemorrhage nor ulceration, and no further abnormalities were detected.

A blood count on July 21 showed: Hb, 42% ; white cells, 27,700 per c.mm (polymorphonuclear leucocytes 2%, cells of lymphocytic series 98%). Blood film:—Red cells showed anisocytosis, but were well filled. There was no evidence of red-cell regeneration. The lymphocytic series was made up largely of lymphoblasts, but some degenerating " smudge " cells were also present. The granulocytes were of the early type. Platelets were few. The whole blood picture was highly suggestive of acute lymphoblastic leukaemia.

The count was repeated two days later, when the haemoglobin level had fallen to 28%. The clinical condition had markedly deteriorated, and the child was wretched with buccal ulceration

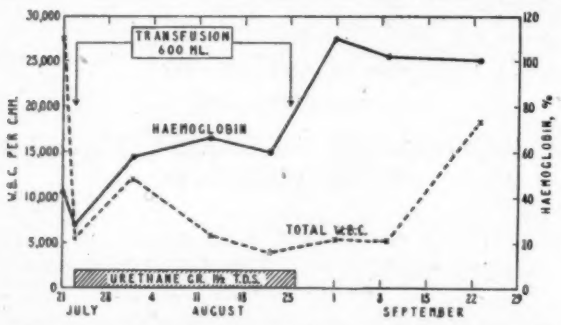
and was having haematemesis and melaena. The temperature rose intermittently to 102° F. (38.9° C.), and the pulse to 160.

As death appeared imminent from blood loss, 600 ml. of Group O blood was transfused, with marked clinical improvement, on July 23. The same day urethane, 1½ gr. (0.1 g.) thrice daily orally, was started.

The succeeding blood counts are shown in the accompanying Table and Chart. The changes in the blood picture were associated with slow but definite clinical changes from a moribund condition to that of a child behaving normally for its age. She was now apyrexial, and although the cervical lymph glands could still be palpated they were considerably smaller. On Aug. 22 the leucocyte count had fallen to 4,000 per c.mm., with 61% polymorphs. Urethane was discontinued, a total of 51 gr. (3.25 g.) having been given over 34 days. A further transfusion of 600 ml. of Group O blood was given to combat leucopenia.

Record of Blood Counts

Date	Hb %	W.B.C. per c.mm.	Polymorphs, %	Metamyelocytes, %	Lymphoblasts, %	Lymphocytes and "Smudge" Cells, %	Monocytes, %
21/7/47	42	27,700	2	—	98		—
23/7/47	28	5,500	4	0·5	12	83·5	—
1/8/47	58	11,900	37	—	2·5	58·5	2
13/8/47	66	5,700	60	0·5	2	32	5·5
22/8/47	60	4,000	61	—	—	35	4
1/9/47	110	5,400	42	—	—	57	1
9/9/47	102	5,200	67·5	—	—	30	2·5
23/9/47	100	18,150	76·5	2·5	—	18	3



The apparent recovery of the child called for a reconsideration of the diagnosis. A Paul–Bunnell test for glandular fever proved negative. When sent home on Sept. 28 the child appeared to be quite well.

Unfortunately she was not seen as an out-patient because she lived 50 miles away, but in a reply to a letter her private doctor stated that "she went downhill rapidly and died on Oct. 27."

Discussion

Watkins (1947) states that in acute leukaemia of children little or no benefit is obtained from urethane, and that there is not sufficient change to warrant its use other than experimentally. Undoubtedly in my case blood transfusion was a life-saving measure at first, but the dramatic clinical and haematological improvement was far greater than could have been due to transfusion alone. Spontaneous remissions are not uncommon after transfusion in acute leukaemia of children, but a remission rarely lasts more than a week, and the disease is usually fatal within two months of the onset. In the present case the improvement after transfusion was maintained, and would appear to have been enhanced and prolonged by urethane treatment.

The prognosis was exceedingly grave in view of the child's age and of the fall in haemoglobin level to 28%. Paterson *et al.* (1946) attach importance to the initial haemoglobin level, for in three out of four of their cases of lymphatic leukaemia in which the haemoglobin was below 55% the patient died despite adequate blood transfusions.

It is unfortunate that no blood count was done when the final deterioration began, as it is now impossible to say whether this was due to an exacerbation of the original disease or to the toxic effect of urethane on the myeloid cells. This was foreshadowed in the blood count of Sept. 23, when of 18,150 white cells 2.5% were metamyelocytes and 76.5% were young band forms of polymorphonuclear leucocytes.

The use of urethane in this case profoundly modified the disease process, and therefore seems to have been justified.

Summary

A case is described of acute lymphoblastic leukaemia which responded initially to urethane therapy.

The palliative effect in this case would seem to justify further trials of urethane in acute leukaemia.

It is uncertain whether the fatal outcome in the case described was due to the disease or to the toxic effect of urethane on cells of the myeloid series.

Whilst it is probable that the large volume of blood given to this child contributed largely to the remission in the leukaemic state, it seems reasonable to suppose that the duration of this remission was related to the use of the drug.

My thanks are due to Dr. E. D. Scott and Dr. M. A. Leslie-Smith for permission to publish the case, and to Dr. S. Instone for her encouragement and advice.

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Medical Memoranda

Malignant Tumour of the Small Intestine

Malignant tumours of the small intestine are relatively uncommon, although reports on more than 500 cases are now available. Carcinoma is said to occur more often than sarcoma in the proportion of 6 to 4 (Mayo, 1940), carcinoma being found most commonly in the jejunum and sarcoma in the ileum. The age incidence in carcinoma is accepted to be higher than in sarcoma, and the sex incidence is in favour of males in the ratio of 2 to 1.

The following report of a case of adenocarcinoma of the ileum differs from those recorded by Rankin and Mayo (1930) in that no loss of weight occurred and no occult blood was found.

Case Report

A publican aged 59 was admitted on Jan. 6, 1948, complaining of generalized abdominal pain and vomiting. His symptoms first began 11 months previously, and consisted of griping pains and vomiting in attacks lasting 10 to 14 days. He suffered some half-dozen such attacks, with intervals of about a month's freedom, before consulting his doctor. Two days before admission he developed generalized abdominal pain with vomiting and for the first time he had absolute constipation.

During the 1914–18 war he contracted malaria and sandfly fever while serving in Palestine. Since that time he had always had two or three loose motions daily, but at no time did he notice blood or mucus in the stools. He suffered for many years from winter bronchitis.

On examination he was seen to be a well-built man with no obvious loss of weight. He was in considerable pain and was vomiting at fairly frequent intervals. The abdomen showed a generalized distension, with some diffuse tenderness on palpation, but no mass was felt. He had shifting dullness in the flanks, and loud borborygmi were heard. Rectal examination showed no abnormality. He was given an enema, which produced a faecal result in the form of a foul-smelling, pale, toothpaste-like ribbon. A further enema one hour later was returned unchanged, and a diagnosis of intestinal obstruction was made, the cause of which was not obvious.

Operation.—The abdomen was opened through a lower right paramedian incision and a quantity of straw-coloured fluid escaped from the peritoneal cavity. There was marked distension of the small intestine down to a point 30 in. (76 cm.) from the ileo-caecal valve.

A hard mass about the size of a tangerine orange involved the gut at this point and occluded the lumen of the bowel. A resection of 8 in. (20 cm.) of the bowel including the tumour, together with a wedge of mesentery containing enlarged glands, was carried out, continuity being restored by lateral anastomosis. The anastomosis was performed first, as the patient's condition had deteriorated, but as it subsequently improved resection became possible. The abdomen was closed and the patient returned to bed with an intravenous glucose-saline drip and a gastric aspiration in operation.

Pathology of the Tumour-bearing Intestine.—"The loop of small intestine is involved by a stenosing carcinoma of scirrhous appearance. The tumour is about 1 in. (2.5 cm.) in length and encircles the whole wall. No gross ulceration of the mucosa is observed and no polypi are seen. Careful search fails to reveal any associated lymph glands involved by metastases. Histological examination showed an adenocarcinoma which is deeply infiltrating the bowel wall, with an accompanying scirrhous reaction. The lesion is not of carcinoid origin, the tumour consisting of acini of varying size, showing irregularity in cell type and nuclear configuration."

Convalescence was lengthened by a post-operative pneumonia but was otherwise uneventful, and the patient was discharged on Jan. 23. When last seen two months later he was well and leading a normal life.

I am indebted to Mr. G. F. Mitchell, under whose care the patient was admitted, for permission to publish this case, and to Dr. R. L. Bishton and Dr. R. C. Hill for the pathological report on the specimen.

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A Case of Inherited Spina Bifida

The aetiology of foetal deformity is still uncertain. Such diverse factors as heredity, multiparity, diabetes, placenta praevia, and maternal rubella have variously been incriminated. The inheritance of minor deformities along Mendelian lines is not uncommon; while the occurrence of a major deformity in siblings increases the chance of such deformity reappearing, though Gibberd (1947) considers this to be only a fourfold increase above the normal probability. Direct inheritance of major deformity from the mother is naturally uncommon, and the following example is worthy of record.

CASE HISTORY

A primigravida aged 21, in her 37th week of gestation, was admitted to hospital on May 7, 1947, with diagnosis of toxaemia and disproportion. The toxaemia proved to be minimal, but examination disclosed a fluctuant swelling the size of a coconut in the midline of the lumbar region, extending from the second lumbar to the first sacral vertebra. There was exaggeration of the lumbar lordosis, but no scoliosis; the swelling was compressible and had a well-marked cough impulse. Both feet showed pes cavus (right more than left). There was wasting of the thigh and calf muscles on the right, and ¾ in. (1.9 cm.) shortening of the right lower extremity. A diagnosis was made of meningomyelocele, and the spinal deformity was confirmed by radiography at a later date.

Obstetrically, the case was one of brim disproportion, with a floating head and some slight degree of hydramnios. *X*-ray examinations were intended, but labour started spontaneously the night after admission, and vaginal examination soon showed that the disproportion was caused by a hydrocephalic head; this was perforated at half dilatation of the cervix, and a female foetus weighing 6 lb. 1 oz. (2.75 kg.) was delivered uneventfully. It showed a moderate hydrocephalus, with a gross dorsi-lumbar spina bifida of the open myelocele type.

COMMENT

No reference to the inheritance of spina bifida has been found in the available literature, and Ford (1946) does not include it in an exhaustive list of inherited disorders. Despite the difference in degree of the foetal and maternal condition it seems reasonable to suppose that some genetic factor had been transmitted and that further pregnancies would run a very considerable risk of being similarly affected. It is impossible to assess the relative importance of heredity and environment in relation to the developmental errors of the young embryo; the majority of gross abnormalities are lost as abortions, while of those which are born alive only a very small percentage reach reproductive life and have the opportunity of passing on to the next generation whatever genetic factor may be involved. There is a growing tendency to find environmental factors such as dietetic deficiency (Warkany, 1944), rhesus iso-immunization (Wiener, 1946), and maternal rubella (Gregg, 1941) to account for foetal deformity, but it seems probable that many cases of gross defect are genetic in origin.

My thanks are due to Mr. Samuel Davidson for permission to publish this note.

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Occurrence of Convulsions During Treatment with Calciferol

The value of high dosage of calciferol in the treatment of lupus is well established, and in view of the success of the method its use is likely to be further extended until the therapeutic effect has been evaluated in other tuberculous infections. Calciferol has been recognized as a potentially toxic drug, and anorexia, nausea, vomiting, and polyuria are well known to follow its use. So far, however, I have seen no record of the occurrence of convulsions after calciferol and therefore consider that the following case should be put on record.

CASE HISTORY

A boy aged 10 was admitted to the Surrey County Hospital with a history of malaise for one month and an unexplained pyrexia of one week's duration. On admission the temperature was 101° F. (38.3° C.). The abdomen was full and slight tenderness was present on deep palpation in the R.I.F. No definite mass was felt, but on bimanual examination with a finger in the rectum a large gland was discovered low in the right side of the abdomen. White cells numbered 7,500 per c.mm. (P. 70%, L. 20%, M. 9%, E. 1%). The Mantoux test was positive 1 in 10,000. *X*-ray examination of the chest revealed nothing abnormal. A diagnosis of tuberculous mesenteric adenitis was made, and treatment with calciferol 50,000 units twice daily was started. The temperature settled rapidly, with an occasional evening rise to 99° F. (37.2° C.). On Nov. 21, 1947, the boy was allowed home at his parents' request, to rest in bed and continue calciferol, 50,000 units twice daily. There had been no symptoms of intolerance during his stay in hospital, but the parents were warned of the possible occurrence of toxic symptoms. On Dec. 15 he was readmitted to hospital suffering from generalized convulsions. It appeared that, in addition to the 100,000 units of calciferol prescribed, an ampoule of sterogyl containing 600,000 units had been given by mouth a week previously. Soon afterwards nausea, occasional vomiting, and obstinate constipation had developed; he became increasingly drowsy and could not be roused for some hours before the first convulsion began.

On admission very frequent generalized convulsions were occurring; no focal signs were present on examination of the central nervous system except for an extensor plantar response on the right side, which became flexor 48 hours later. Treatment included 0.25 g. of soluble hexobarbitone intravenously, followed by 1½ gr. (0.1 g.) of soluble phenobarbitone intramuscularly two hours later. Apart from a further slight convulsion and slight vomiting recovery was uninterrupted, being complete in 48 hours. The blood calcium was 18 mg. per 100 ml. on the day of admission, falling to 14.8 on Dec. 22 and 12.9 on Dec. 29. The urinary output was well maintained and the urine contained no albumin or casts. The blood urea was not estimated.

There was no family history of fits, nor had the boy suffered previously from convulsions.

COMMENT

In view of the fact that increasing concentrations of calcium are known to decrease the frequency of impulses discharged from nerve cells stimulated with acetylcholine it seems likely that the fits were due to a direct toxic effect of calciferol rather than to the associated hypercalcaemia. Overdosage with calciferol is known to produce a rise in the blood urea, but in the absence of oliguria or albuminuria it seems unlikely that the convulsions were uraemic in origin.

HEWARD BELL, M.B., M.R.C.P.

Reviews

GENITO-URINARY SURGERY

Textbook of Genito-Urinary Surgery. Edited by H. P. Winsbury-White, M.B., Ch.B., F.R.C.S., F.R.C.S.Ed. With 39 Eminent Contributors. (Pp. 1046; 451 illustrations, many in full colour. £4 10s.) Edinburgh: E. and S. Livingstone. 1948.

There can be no doubt of the importance of this book. It is the first work written by many authors that has come from the British school of genito-urinary surgery, and as such it is sure of a welcome. To edit such a book is no light undertaking, and any criticisms of this impressive volume are made with a full realization of the arduous work that its production must have entailed for Mr. Winsbury-White.

One of his many difficulties must have been to select the contributors, of which there are thirty-nine. A skilful surgeon is not necessarily a clear exponent of his art, and even if he can write he may be tempted to give undue prominence to the methods of treatment he favours and to the particular technique he uses in operating, thus giving an unbalanced account of the subject he discusses. It is risks of this kind that an editor in command of so large a team must take. Inevitably the various contributions to this work are of unequal value, and it would be invidious to try to compare the quality of the different sections. All that can be said is that the editor has chosen contributors that are good representatives of British genito-urinary surgery, although one or two names we might have expected to see are missing. It would have been more convenient if the names of the various writers had appeared at the beginning of their articles instead of being tucked away at the end of them. So also might it have been preferable if such a bulky and heavy tome as this had been broken into two volumes, but the shortage of boards and the scarcity of binders may well have made this difficult. The illustrations and the coloured plates are of a very high order. The need for an up-to-date work by British urologists has long been apparent, and we confidently expect that this handsome volume will find a place on the bookshelves of a great many surgeons, not only here in England but abroad.

KENNETH WALKER.

MEDICAL RESEARCH IN AMERICA

American Medical Research Past and Present. By Richard H. Shryock, Ph.D. Studies of the New York Academy of Medicine Committee on Medicine and the Changing Order. (Pp. 350. 14s.) New York: The Commonwealth Fund. London: Geoffrey Cumberlege. 1947.

This book is something new and exciting in medical literature. The author is a non-medical professional historian. It is essentially a social history of medical research which relates the development of medical research in the U.S.A. to the economic progress of society. There have been four phases in American medicine: the British influence from 1750 to 1820, the French from 1820 to 1860, the German from 1860 to 1895, and the independent American tradition thereafter. Until the end of the nineteenth century the mainspring of American life was commerce and the pursuit of wealth, and none of the disinterested arts—painting, music, or medical research—really flourished there. The turning points were the growing realization of the importance of science to national life and industrial prosperity, the foundation of the Johns Hopkins Hospital, which set a new pattern for medical education in America, and the Rockefeller bequests, which directly and indirectly stimulated the expansion of medical research.

Dr. Shryock discusses with dispassionate understanding many problems that still beset us—the difficulty of securing adequate rewards for teaching and research in a competitive society, the arguments for and against security for the research worker, the difficulties of team work, the problems of planning research in a free society. There are signs that in America also the era of private support for research is coming to an end owing to the diminishing number of large incomes under individual control. The State is becoming more and more the dominant partner in subsidizing research. It has been estimated that, whereas just before 1940 total expenditure on all forms of scientific research in the U.S.A. was about $250,000,000, of which only $50,000,000 were Federal funds, by 1944 more than $600,000,000 was being spent by the Federal Government alone. It has even been suggested that research should be established as a fourth branch of government. These developments have given rise to the usual fears of the regimentation of science, and the usual controversy for and against planning of work and of the relative importance of fundamental and applied science. Dr. Shryock's book is therefore more than a history of American medical research: it is a discussion of the basis and philosophy of research in general. It is clearly written and closely documented, and will be of the greatest value to all who benefit from, take part in, or make provision for medical research.

L. J. WITTS.

LECTURES ON PSYCHO-ANALYSIS

Lectures on Psychoanalytic Psychiatry. By A. A. Brill, Ph.B., M.D. (Pp. 259. 15s.) London: John Lehmann. 1948.

This book can be recommended without reservation. Unlike so many publications purporting to describe psycho-analysis it is an authoritative work written by the acknowledged founder and mainstay of psycho-analysis in the U.S.A., who until the day of his death practised and taught Freudian analysis with unswerving devotion to its principles. It consists of a series of lectures given annually to audiences of young psychiatrists for close on a quarter of a century. Based on a ripe experience of both psycho-analysis and psychiatry, and written in a clear and almost racy style, it can be read with understanding by any intelligent layman wanting to acquire some orientation in both subjects.

Of particular interest to the general reader is the introductory chapter, in which Brill describes the state of psychiatry when, shortly after his qualification, he made his first approach to the subject. The descriptive psychiatry of Kraepelin, which, thanks to the exertions of Meyer, was then much in vogue, soon left Brill dissatisfied, and a journey to Paris in search of more effective therapeutic methods was equally disappointing. At this point, Brill tells us, he nearly threw up the sponge; but a lucky recommendation to visit Burghölzli, where Bleuler together with Jung and others were investigating the theories of Freud some twelve years after they were first adumbrated, led to his complete conversion to the psycho-analytical approach. Incidentally, his asides on Jung's belligerent and irascible devotion to Freud are particularly intriguing in the light of Jung's later repudiation of Freud and all his works, or at any rate his abandonment of all that mattered in psycho-analysis. In these days, when newcomers to psychiatry are inclined to take for granted that the discoveries of Freud were just an important part of a general psychiatric progress, it is well to be reminded so uncompromisingly that Freud was the founder not only of psycho-analysis but of modern clinical pyschology.

EDWARD GLOVER.

EARLY MEDICINE IN INDIA

The Beginnings of Modern Medicine in Madras. By D. V. S. Reddy, With foreword by Major-General J. B. Huban, Surgeon-General with the Government of Madras. (Pp. 240. 5 rupees.) Calcutta: Thacker, Spink and Co. (1933), Ltd. 1947.

Dr. Reddy's book is an interesting and very readable addition to the history of medicine in the Madras Presidency from the early days of the ship surgeons of the East India Company to the dawn of modern medicine there—the foundation of the Madras Medical School in 1835, the precursor of the present institutions, hospitals, colleges, and laboratories in the Presidency. The author dedicates his book to his teachers in the Madras Medical College and associated teaching hospitals, and in the opening words of his preface he says that this work, based on the study of original records, is the outcome of his love and gratitude to his alma mater, the Madras Medical College, and its parent institution, the Madras General Hospital—institutions that have trained thousands of medical men and saved the lives and health of millions of mankind, men, women, and children, of all nationalities and creeds. Nor in the reviewer's opinion is his claim exaggerated, for at the Madras

General Hospital there is probably a greater wealth of available medical material relating to tropical medicine than at any hospital in the world and an atmosphere as democratic as that in any large London hospital. One reason is that Madras has a longer history of close association with the West than any other part of India; it is almost the only part of that sub-continent where a large European, Eurasian, and native Christian community has long been naturally domiciled. The result has been that modern medicine has had a very favourable soil in which to develop.

In a prologue the author describes very briefly the general evolution of medicine, outlining its sources from Graeco-Roman, Arab, Ancient Indian, and Western European systems; he fixes the date for the beginning of modern medicine as barely 300 years ago. When the first ships from Europe touched the West Coast of India towards the close of the fifteenth century India was, as the author points out, neither then a vast dark continent like Africa nor devoid of medical practitioners, as the edicts of Asoka and other records show. Nevertheless, modern medicine came from the West. Beginning with an account of the medical arrangements of the East India Company, he describes its history in those early days during which medical organization and technical advance passed by slow stages and often through troublous times to what blossomed forth into the modern medical institutions that now serve the needs of fifty millions of multitudinous race, creed, and social status.

RICKARD CHRISTOPHERS.

GUIDE FOR STUDENTS

The Clinical Apprentice. A Guide for Students of Medicine. By John M. Naish, M.D., M.R.C.P., and John Apley, M.D., M.R.C.P. With foreword by Professor J. A. Ryle. (Pp. 200; 71 illustrations. 15s.) Bristol: John Wright and Sons. 1948.

This book is one of the best and one of the shortest of the many which undertake to guide the footsteps of the student newly entered upon his clinical career. The approach throughout is clinical in the strictest etymological sense, and the patient, instead of being disarticulated into a collection of unrelated systems, is allowed the privilege of remaining an indivisible whole. The authors have omitted any discussion of clinical pathology and the arid pages of anatomy and physiology which encumber so many books of this type. In simple, almost colloquial language, with a leaven of equally simple humour, they introduce the student to his first patient and explain the basic principles of physical examination. This lively and unpretentious little book provides the clinical clerk with just what he needs during his first few weeks in the medical wards without arousing despondency by revealing too clearly how much he has to learn.

R. BODLEY SCOTT.

The Hospitals Year-Book 1948 (British Hospitals Association, 52, Green Street, W.1; £1 1s.) is mainly a directory assembling a mass of useful information about the regional hospital boards, the grouping of hospitals under management committees, and the designated teaching hospitals under boards of governors. The list of hospitals disclaimed from the National Health Service by the Minister of Health is given. There are 256 of these, the majority being small or of a denominational character. The *Year-Book* also sets out the hospitals as they were on July 4, 1948. The statistical tables of the work and finances of the voluntary hospitals before the taking-over are now a closed chapter, but they have their interest. In particular it is shown what a tremendous financial burden the steeply rising costs became. The cost of the voluntary hospitals for maintenance alone rose by 115% between 1938 and 1946. However, there was a large increase in voluntary contributions under the shadow of impending change. The increase in cost was not confined to voluntary hospitals: municipal and mental hospitals show comparable increases. The editor, Mr. J. P. Wetenhall, suggests that the risk of remote control is by no means yet a thing of the past, although the position has been considerably safeguarded by the final form of the Act and by certain subsequent regulations which imposed a considerable measure of responsibility on the new hospital management committees. It is clear from this compilation that there is a great public interest in hospitals and a desire on the part of many to do personal service. A constitution for Leagues of Friends, through which active interest and support for local hospitals may be rallied and maintained, has been drawn up by the British Hospitals Association.

BOOKS RECEIVED

[*Review is not precluded by notice here of books recently received*]

Die Weiblichen Sexualhormone in der Pharmakotherapie. By O. Mühlbock and others. (Pp. 300. 24.80 Swiss francs.) Berne: Hans Huber. 1948.

The chemistry, pharmacology, and therapeutic uses of the female sex hormones.

Höhenklima-Forschungen des Basler Physiologischen Institutes. Edited by F. Verzar. 2nd ed. (Pp. 97. No price.) Basle: Benno Schwabe. 1948.

Papers on physiological changes at high altitudes.

Les Facteurs Vasculaires et Endocriniens de L'Affectivité. By A. M. P. Abely and others. (Pp. 190. 400 francs.) Paris: L'Expansion Scientifique Française. 1948.

A study of the physiological changes that may accompany affective disorders.

Schicksalsanalyse. By L. Szondi. 2nd ed. (Pp. 422. 28.50 francs.) Basle: Benno Schwabe. 1948.

Analysis of the individual's destiny in relation to his mental inheritance and family environment.

Heredity in Essential Hypertension and Nephrosclerosis. By P. Söbye. Vol. 16. (Pp. 225. No price.) Copenhagen: Arnold Busck. 1948.

The author concludes that the development of these disorders is probably always due to a hereditary gene.

Hungerkrankheit, Hungerödem, Hungertuberkulose. By A. Hottinger and others. (Pp. 297. 28 francs.) Basle: Benno Schwabe. 1948.

The pathological and clinical effects of starvation and its consequences.

Gadd's Synopsis of the British Pharmacopoeia. By H. W. Gadd. 15th ed. (Pp. 249. 5s.) London: Baillière, Tindall and Cox. 1948.

A summary of the 1948 *B.P.*, with notes on the law relating to poisons and dangerous drugs.

A.M.A. Interns' Manual. Issued by the American Medical Association. (Pp. 201. 12s.) London: W. B. Saunders. 1948.

Notes on laboratory tests and on the uses and prescription of the commoner drugs.

Health Teaching in Schools. By R. E. Grout, M.P.H., Ph.D. (Pp. 320. 20s.) London: W. B. Saunders. 1948.

A manual for school teachers.

Clinical Studies of Besnier's Prurigo. By P.-H. Nexmand. (Pp. 236. No price.) Copenhagen: Rosenkilde and Bagger. 1948.

A monograph on the disorder, with special reference to its treatment.

The Principles and Practice of Rectal Surgery. By W. B. Gabriel, M.S., F.R.C.S. 4th ed. (Pp. 508. 45s.) London: H. K. Lewis. 1948.

The text has been revised and a new chapter on anal incontinence included.

Dictionary of Genetics. By R. L. Knight, D.Sc., Ph.D., A.I.C.T.A. (Pp. 183. $4.50.) Waltham: Chronica Botanica. 1948.

Includes terms used in cytology and animal breeding.

Morals in the Melting Pot. By E. F. Griffith, M.R.C.S., L.R.C.P. (Pp. 295. 9s. 6d.) London: Methuen. 1948.

The author discusses such topics as contraception, divorce, extra-marital relationships, homosexuality, and preparation for marriage.

Human Physiology. By C. G. Douglas, C.M.G., *M.C.*, D.M., F.R.S., and the late J. G. Priestley, *M.C.*, D.M. 3rd ed. (Pp. 258. 18s.) London: Geoffrey Cumberlege. 1948.

A practical course for the student of physiology.

The Narrow House. By H. Fernee. (Pp. 272. 8s. 6d.) London: Christophers. 1948.

A thriller set in Soho.

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HAEMOLYTIC DISEASE OF THE NEWBORN

Haemolytic disease of the newborn continues to be the subject of intensive research, and advances in knowledge of two kinds have been published recently. In the first place the predictions of Fisher have been confirmed by the discovery by independent observers of both anti-d serum[1] and the CdE (Rh_y) type.[2] It is therefore probable that the boundaries of the Rh antigen-antibody scheme are now fully revealed, though within those boundaries Race and his co-workers have displayed in the elementary antigens C, c, D, and probably also E a complexity of antigenic structure at first unsuspected. In spite of lack of agreement on the terminology to be employed, whether the Rh-Hr or the CDE/cde system is the better, it is accepted on both sides of the Atlantic that the Rh group is of complex structure built up from a number of alternative components each of which may on occasion prove antigenic in those from whose constitution it is absent. Lack of agreement on nomenclature does not conceal the essential agreement on the facts now accepted by all workers in this field, who, whatever symbols they may use, realize that they are working with the same components.

The second type of advance is well exemplified by the authoritative paper by Dr. P. L. Mollison and Miss Marie Cutbush published in this issue of the *Journal*. While the fundamental cause of haemolytic disease of the newborn lies in the iso-immunization of the mother against a blood-group antigen which she herself lacks, Rh incompatibility being by far the most common cause, there has been a great deal of uncertainty about the exact mechanisms concerned and about when and how to treat the affected infants. Mollison and his co-workers have done more than anyone to fill in some of these gaps in our knowledge and understanding. The present publication supplements their earlier work on exchange transfusion[3] and on physiological jaundice of the newborn,[4] and provides for the first time easily accessible criteria of severity which every obstetrical unit should be able to determine. A group of 52 normal infants served as controls for 74 affected infants born to immunized Rh-negative mothers. Sixty-nine of the latter group were live-born, and of these 50 were seen on the day of birth. The tests included examination of the blood for haemoglobin and bilirubin content, and the direct Coombs test for sensitization of the red cells. In 41 of the affected infants the serum was also tested for free Rh antibodies, and in 62 the maternal serum was titrated for both saline-agglutinating and albumin-agglutinating antibodies.

Perhaps the most important observations made by Mollison and Cutbush are those on the prognostic value of haemoglobin estimations in the newborn and their significance in determining the line of treatment required. They confirm the substantial rise in haemoglobin levels a few hours after birth brought about by reflux of blood from the placenta and show that anaemia in the newborn can thereby be concealed; capillary blood samples invariably gave higher readings than cord or post-natal venous blood. In normal infants the haemoglobin or cord blood has values of 14–19.4 g. per 100 ml., the mean value being 16.35 g.; within 24 hours the mean value rises to 18.45 g. if placental reflux has been permitted. Of 30 affected infants 14 had cord-blood values within the normal range, and none of these died; 16 had lowered values, and it is noteworthy that only two out of eight infants with less than 8 g.% of haemoglobin survived. When venous blood was examined a few hours later two infants with subnormal values in the cord blood were found to have values within the normal range of infants not recovering placental blood, and this increase was even greater in capillary blood. It is therefore clear that assessment of anaemia in the newborn is much more accurately made on cord-blood samples than on post-natal venous or capillary blood. If only the latter are examined the extent of the haemolytic process may be underestimated and decisions about treatment might be adversely influenced. Some correlation also exists between the degree of anaemia and erythroblastaemia; infants with less than 10 nucleated red cells per 100 white cells had usually over 12 g.% of haemoglobin, and all of these recovered. On the other hand, 15 infants died among 33 whose nucleated red cells numbered more than 20 per 100 leucocytes; primitive forms were abundant, and in all except one the haemoglobin was below 12 g.%.

Another important criterion of severity is the bilirubin content of the blood. In normal infants the values lie between 0.8 and 2.6 mg.% (average 1.6 mg.%), whereas in affected infants the cord-blood bilirubin is raised, indicating that increased haemolysis has been going on *in utero*. Cappell[5] drew attention to the pronounced yellow colour of the umbilical cord in affected children, an observation which may first attract the obstetrician's attention to the disease in the absence of generalized icterus. The level of cord-blood bilirubin has some prognostic significance, for six out of 11 infants with more than 4 mg.% died. In mildly affected infants left untreated, whose cord bilirubin values ranged from 1 to 3.7 mg., the amount in the venous blood rose between the second and fifth days of life to 1.3–15.8 mg. Obviously, therefore, blood bilirubin levels are of prognostic importance only if the estimation is made on cord-blood samples.

In earlier studies Mollison[4] brought forward evidence that the rate of destruction of erythrocytes does not increase after birth, being normally about twice as rapid in the first 10 days of life as at later ages. Physiological jaundice of the newborn is therefore largely due to functional inadequacy of the liver, and anaemia in the neonatal period, as Faxan[6] and Shapiro and Bassen[7] showed, is largely due to insufficient replacement of the destroyed cells. In haemolytic disease the rate of blood destruction is maximal at birth, and the rapid onset of symptoms is due to the physiological stresses attendant upon the establishment of a separate existence.

Wiener[8] claimed that the type of foetal disease could be accurately predicted from the nature of the maternal antibodies, Rh saline agglutinins being associated with icterus gravis, erythroblastosis, and kernicterus, whereas Rh albumin agglutinins were found in cases of hydrops and congenital anaemia. These views found little or no favour with other workers, but Wiener[9] has recently modified them so that he now attaches little or no clinical importance to the presence of Rh saline agglutinins alone in the maternal serum and attributes all forms of haemolytic disease to the presence of antibodies of the albumin-agglutinating type, which he prefers to call univalent antibodies or glutinins. Wiener suggests that only univalent antibodies are capable of traversing the placenta, and he claims that their titre in the maternal blood is closely correlated with the severity of the resulting foetal disease: when the foetus is Rh-negative, and therefore unaffected, the univalent Rh antibody titres of maternal and cord serum are equal, but when the foetus is Rh-positive the foetal red cells become coated by adsorption of the antibodies, the titre in the foetal serum being thereby reduced. Wiener applies this concept also to cases of sensitization to A or B, holding that these are due to the development of immune univalent anti-A or anti-B; he explains the absence of haemolytic disease in most heterospecific pregnancies by failure of the normal isoagglutinins α and β to pass through the placenta in sufficient amount to cause harm.

Mollison and Cutbush, on the other hand, are less satisfied that there is any close correlation between the maternal antibody titre and the prognosis for the foetus. They agree that a high titre of albumin-agglutinin is usually associated with severe anaemia and is a bad prognostic sign, but the converse is not true and many exceptions are encountered. Cases with predominantly saline agglutinins are usually less severely affected, and none of these infants died within the first 24 hours. They stress the impossibility of separating cases sharply into the three main varieties of hydrops, icterus gravis, and congenital anaemia, and consider that these merge imperceptibly the one into the other. Their experience of titrating the Rh antibodies in the infant's serum is also rather different from Wiener's,[10] and they found the amount of free antibody very poorly correlated with the severity of the haemolytic process—one infant with a titre of 1 : 16 was so mildly affected as to require no treatment, though the cells gave a positive direct Coombs test, while others died within 24 hours in spite of a very low titre. On the whole they favour the view that albumin agglutinins are all-important in the aetiology of the disease, since this is more in agreement with their conception of maximum haemolysis before and at birth rather than with the onset or aggravation of haemolysis after birth. In such a view none of the varieties of haemolytic disease is due to entry of maternal antibodies into the foetal circulation only during labour, nor is it necessary to postulate that the effects of blocking antibodies are increased by "conglutinin" rapidly produced after birth. Wiener's conception of this process is at variance with the morbid anatomy of the disease, as Cappell[11] emphasized.

In Mollison and Cutbush's series, out of 69 live births 50 infants survived, and of these only one has shown signs of cerebral damage; whereas in those dying on the second to the fifth days nuclear jaundice was commonly present. Without doubt this complication greatly diminishes the chance of survival, but, as Parsons[12] has pointed out, this is not to be deplored. Although these infants were anaemic at birth, in some this was no longer apparent at the time of death, and a marked erythroblastaemia was evidence of rapid regeneration of red cells in some cases. Mollison and Cutbush do not accept the idea of damage to the central nervous system by the direct action of Rh antibodies on tissue cells. Their work suggests that the three forms of haemolytic disease are merely manifestations of different degrees of haemolysis. If this has been severe and long-continued before birth the foetus is profoundly anaemic and hydropic and is either stillborn or dies within 24 hours, before there is time for severe jaundice and kernicterus to develop. If the process is less severe the infant may live over the first few days, when the excessive haemolysis and functional immaturity of the liver lead to accumulation of bilirubin and other waste products formerly excreted through the placenta; damage to the liver may follow, and this in turn may play a part in determining the occurrence of cerebral damage. The mildest cases of all, the congenital anaemias, are those in which jaundice is not severe but anaemia of varying degree develops. The paradox of absence of severe jaundice but with progressive anaemia may be partly explicable by less severe blood destruction than in icterus gravis together with a more efficiently functioning liver, while the anaemia is probably attributable not only to some excess haemolysis but perhaps even more to an exaggerated depression of haemopoiesis such as Shapiro and Bassen[7] have shown to be concerned in the anaemia of normal infants in the neonatal period. If, therefore, haemolytic disease is due solely to the effects of the albumin agglutinins, it is a little surprising that there is not a better correlation with the titre of such antibodies in the maternal serum, and perhaps there may be some further type of antibody concerned, as Hill, Haberman, and Jones[13] have suggested.

Mollison and Cutbush have demonstrated clearly the great value of the direct Coombs test, which they found invariably positive in affected infants; furthermore, the strength of the reaction was fairly well correlated with the maternal titre of albumin agglutinins and was to some extent of prognostic significance, in so far as a weakly positive reaction was not found in any severely affected infant. The converse, however, was frequently observed, and it is surprising to learn that the direct Coombs test may remain positive, in infants not treated by exsanguination transfusion, for longer than 93 days. If the transplacental passage of Rh antibodies is regarded as an example of passive immunization it would appear that when the cells are destroyed the antibody may be dissociated from the antigen in a form which is capable of

1 Haberman, S., *et al.*, *Blood*, 1948, **3**, 682.
2 van den Bosch, C., *Nature*, 1948, **162**, 781.
3 *Lancet*, 1948, **2**, 522.
4 Ibid., 1948, **1**, 513.
5 *British Medical Journal*, 1946, **2**, 641.
6 *Acta paediatr., Stockh.*, 1937, Suppl. 1.
7 *Amer. J. med. Sci.*, 1941, **202**, 341.
8 *Amer. J. clin. Path.*, 1946, **16**, 477.
9 *Proc. Amer. Ass. Blood Banks*, August, 1948 (in press).
10 *J. Lab. clin. Med.*, 1948, **33**, 181.
11 *Brain*, 1947, **70**, 486.
12 *Lancet*, 1947, **1**, 534.
13 *Blood*, 1948, Spec. Issue **2**, 80.

attaching itself to new Rh-positive cells, and thus the Coombs test may remain positive for a surprisingly long time. In cases treated by exsanguination transfusion, on the other hand, the return of Rh-positive cells to the circulation is not accompanied by a return of the positive direct Coombs test, and perhaps the removal of the major part of the infant's plasma is a more useful contribution to the treatment than has been realized.

In view of this striking testimony to the value of the direct Coombs test it is worth while to examine the claim by Wiener and Gordon[10] that their plasma-albumin conglutination test is superior because of its greater simplicity and increased sensitivity. When examining the red cells of affected infants, however, Hill and Haberman[12] and also Wiener and Gordon observed the occasional absence of a positive conglutination reaction on the part of cells which gave a positive Coombs test. The latter authors explain this phenomenon as due to the absorption of "conglutinoid" by sensitized foetal red cells coated with univalent Rh antibodies. "Conglutinoid" thus prevents the union of the sensitized erythrocytes with "conglutinin" in a manner analogous to the interference by "complementoid" with the action of complement in a haemolytic system or to the inhibition of agglutinating Rh antibodies by blocking Rh antibodies. Wiener and Gordon admit that the cells thus doubly "blocked" nevertheless gave a strongly positive direct Coombs test. An unprejudiced observer might be pardoned for assuming that this is a point substantially in favour of the British test, which is subject to no such fallacies if the cells are first adequately washed in saline.

Now that the technique of exsanguination transfusion is so widely known and is so easily acquired it is very necessary to have sound criteria for the assessment of severity in cases of haemolytic disease. In studying the indications for treatment Mollison and Cutbush have had all the advantages of a research institution behind them, and by rigorous control of their technical methods they have ensured a standard of accuracy which few laboratories will attain. Even with less rigid standards, however, the relatively simple investigations on which they lay the greatest stress can be undertaken in the majority of hospital laboratories with a sufficient degree of accuracy to bring about a great improvement in the assessment of individual cases, provided only that due care is taken to perform the haemoglobin estimations with properly calibrated instruments and to collect, whenever possible, a sample of cord blood for the initial investigations.

CONTINUING STREPTOCOCCAL DISEASE

The pathogenesis of rheumatic fever is a puzzle, but it is generally agreed that the haemolytic streptococcus plays an important part. In 1930 Schlesinger[1] suggested that repeated streptococcal infection, by altering the tissue reactivity, predisposes an individual to acute rheumatism, and some support to this view is given by Rantz and his co-workers,[2] who have recorded the results of a large-scale investigation carried out during the war by the Commission on Haemolytic Streptococcal Infections of the U.S. Army. Some 1,500 cases were studied, 410 of which were found to have had an invasive streptococcal infection. Rheumatic fever did not develop in any of the 1,100 men with infections definitely or probably not of streptococcal origin, whereas 15 cases occurred among the 410 men with infections due to Group A haemolytic streptococci. But apart from the obvious cases of rheumatic fever the authors noticed that many men, even in the absence of continuing suppurative complications, failed to attain a true measure of health after clinical recovery. After analysing the results of their observations they postulate the existence of what they term a "post-streptococcal state," of which manifest carditis is but the extreme example.

This clinical crescendo may be grouped broadly into four stages. First, patients in whom the only sign of tissue reaction after recovery is a persistently increased blood sedimentation rate. In the second group the increase in sedimentation rate persists during a latent period which is followed by irregular fever and a history of general malaise, tiredness, and loss of weight. Some of these patients may pass into the third stage, in which, though the heart appears normal on clinical examination, changes can be found in the electrocardiogram. Finally, the fully established acute rheumatic arthritis with or without obvious cardiac damage forms the possible end-result of the syndrome. It is interesting that Watson, Rothbard, and Swift[3] reached much the same conclusions from their study of 110 soldiers in 1945.

In a later analysis of 299 streptococcal infections Rantz and his colleagues[4] concluded that 72 patients probably showed some degree of this continuing disease. Arthritis, for example, was seen in 19. Among these there was usually no evidence of an intervening latent period, but in 9 of them abnormalities had appeared in the E.C.G. before the arthritis began. In 14 other patients recovery from the streptococcal infection was followed by a latent period of apparent recovery varying from 15 to 19 days, after which a secondary rise of temperature occurred. All but one of these patients had an increased blood sedimentation rate throughout the latent period, in some for as long as six weeks, and in five of them abnormalities in the electrocardiogram were apparent, though there was no clinical evidence of cardiac disease. Finally, in 10 patients the persistence in the rapidity of the blood sedimentation rate was the only obvious abnormality, yet in four of them the electrocardiogram was abnormal.

When the series was examined with a view to determining the effect of treatment on the subsequent development of this continuing streptococcal disease no difference was discovered between those untreated and those who received chemotherapy with sulphonamides or penicillin; and even when salicylates were used throughout the acute stage the apparent reduction was not sufficiently large to suggest a true difference. It is interesting, however, in view of the attention which is now given to ward reinfection, to find that amongst the patients infected with only one type of

[1] *Arch. Dis. Childh.*, 1930, **5**, 411.
[2] *Arch. Intern. Med.*, 1945, **76**, 131; 1946, **77**, 121, 260, and **78**, 369; 1947, **79**, 272, 401.
[3] *J. Amer. med. Ass.*, 1945, **128**, 1145.
[4] *Arch. Intern. Med.*, 1947, **79**, 401.
[5] *Bull. Johns Hopk. Hosp.*, 1942, **71**, 123.
[6] Ibid., 1944, **75**, 115.
[7] McKeown, E. F., *J. Path. Bact.*, 1947, **59**, 547.

streptococcus the incidence of the post-streptococcal state was 12% ; whereas in those who later were reinfected with one or more new types the incidence was 32%. Schlesinger's insistence on the importance of reinfection thus seems sound.

It is always tempting to try to find a single cause for a clinical syndrome, and in an acute infection the bacterial agent seems the obvious starting point. But it may well be that in certain pathological states it is not the primary infecting agent which matters so much as the reaction which it induces in the host: there are now numerous examples of similar clinical pictures being produced by a variety of agents. Rich's work,[5 6] which relates certain forms of sensitization to the reaction of tissues that is seen in periarteritis nodosa, is an example ; and more recently the demonstration of typical Aschoff bodies occurring as a result of sensitization to horse serum seems an indication of another.[7] As Rantz points out, the post-streptococcal state cannot be due to any type-specific fraction or product of *S. pyogenes*. He believes that typical rheumatic fever is more likely to occur in areas where streptococcal infection is common and where the degree of sensitization is therefore likely to be greater. In suggesting that rheumatic fever should be regarded as the extreme form of a more widespread state of streptococcal reactivity this group of workers has made a valuable contribution to the epidemiology of rheumatic disease.

PROPHYLAXIS OF FILARIASIS

Filariasis is still one of the greatest of the unsolved medical problems of the Tropics. It is true that *Loa loa* produces nothing more serious than Calabar swellings, but the repeated attacks of pain and itching, continuing in some patients for years, have to be endured before they can be realized, and in many areas few escape infection. Onchocerciasis is more serious, for in parts of the Anglo-Egyptian Sudan, the Belgian Congo, and the Gold Coast it is the cause of much blindness. Infection with *Wuchereria bancrofti* also is often serious, since it produces elephantiasis of the limbs and genital organs. This may be a menace not only to health but to social security, for many tribes regard swelling of the scrotum as proof positive that the individual is a witch who has been caught by his own witchcraft.

While it has long been known that antimony salts have some action on microfilariae in the blood, it is only in recent years that new drugs have been found which seem to have some specific action on filarial worms. The search for such drugs has been greatly facilitated by the use of a filarial parasite, *Litomosoides carinii*, parasitic in the cotton-rat. We have already drawn attention[1] to the most promising of these new compounds, 1-diethylcarbamyl-4-methylpiperazine hydrochloride, known commercially as "hetrazan." So far, however, cure is a long and tedious process. In a communication published on page 130 of this issue Drs. W. E. Kershaw and D. S. Bertram and Mr. J. Williamson report experiments which suggest that it may be possible to take a prophylactic drug which will prevent the development of filarial infection. They showed that in cotton-rats *p*-melaminyl phenyl stibonate ("MSb") undoubtedly protects against infection with *L. carinii*. This substance is one of a series of quinquevalent antimonials prepared by Friedheim and his colleagues[2] with the object of obtaining a potent prophylactic against trypanosomiasis. These preliminary observations suggest that for a period up to 21 days MSb is quite efficacious. How long the prophylactic effect of a single injection lasts requires further study. It is of course a far cry from protecting rats against *L. carinii* to finding a reliable prophylactic against human filarial worms, yet worms of the same genus whatever their vertebrate hosts seem generally to be vulnerable to the same or closely allied chemical substances. Soon it will be necessary to inquire into the compatibility of the various drugs which the sojourner in the Tropics will be required to take in order to protect himself against parasitic worms and protozoa.

[1] *British Medical Journal*, 1948, **2**, 32.
[2] *J. Amer. chem. Soc.*, 1947, **69**, 560.

COUGH FRACTURE OF THE RIBS

Although cough fractures of the ribs were first described almost a century ago, this has remained an unfamiliar accident. In this issue of the *Journal* there are two papers on the subject. Dr. R. C. Cohen found the condition in seven tuberculous patients, and this is undoubtedly the variety of cough fracture best known to the profession. Cough fracture occurring in late pregnancy, as described by Drs. J. W. Paulley and A. C. Pearson and Mr. D. H. Lees, is a clinical entity quite unknown to many obstetricians and recognized by only a few. The various factors responsible for cough fractures are discussed by the authors of both these papers ; sudden muscular contraction is undoubtedly the most important, especially at those sites where two large muscle masses exert a pull in different directions—sites such as the junction between the external oblique and serratus anterior muscles and between the latissimus dorsi and external oblique muscles. While the muscle attachments provide a simple explanation of the liability of the lower ribs to be fractured in this way, it is remarkable that the fractures occurring during pregnancy have been almost entirely on the left side. Dr. Paulley and his co-authors suggest two other contributory factors in these cases : first, sharp contraction of a hypertrophied sacrospinalis muscle mass, and, secondly, direct impingement of the uterine fundus on the left lower ribs (the liver apparently protecting the ribs on the right side). Although the latter explanation may at first seem improbable, it is difficult to make any other suggestion which will satisfactorily explain the striking incidence of these fractures on the left side. There can be little doubt that increased awareness of this condition will lead to much larger numbers of cases being reported. Recognition of these fractures in late pregnancy would seem to be a matter of importance : apart from the very troublesome pain to which they may give rise and the possibility of its relief by strapping the chest, it is obviously necessary to differentiate the condition from more serious causes of pain in the chest.

ANTITHYROTOXIC FACTOR OF LIVER

There is considerable evidence that in experimental hyperthyroidism the need for vitamin A, ascorbic acid, and certain factors of the vitamin B complex is increased. Attention has been focused chiefly on the vitamins of the B complex because they have been found to be associated with the enzyme systems which yield energy to the organism. The thyroid gland, through its hormone, appears to exert a regulatory influence on these energy-producing metabolic processes, although the specific

[1] *J. Nutrit.*, 1947, **34**, 431.

function of the thyroid hormone is not clear. It is logical to assume that the increased metabolic rate which results from the administration of thyroid may necessitate an increased intake of the B vitamins. Many of the individual vitamins will give some protection against the loss in weight that occurs in experimental hyperthyroidism, although Betheil and his colleagues[1] at the University of Wisconsin have recently shown that none is as good in this respect as liver, which produces better growth and improves the chances of survival. The antithyrotoxic factor of liver is heat-stable, it is not destroyed by heating with acids or alkalis, and it does not appear to be identical with any of the known B vitamins. Work is in progress at the University of Wisconsin on the fractionation of liver preparations to obtain more information on the properties of this antithyrotoxic factor and to isolate it if possible.

MEAT INSPECTION

Meat inspection in England is far behind what is the practice in many other countries. In a paper read earlier this year at the annual conference of the National Veterinary Medical Association Mr. Horace Thornton[1] made several suggestions for its improvement, but his contention that there had been virtually no change in fifty years will not pass unchallenged. A reduction in the number of slaughter-houses from some 16,000 to under 600 during the war years and the appointment by the Ministry of Food of a team of advisers on meat inspection, mostly veterinary surgeons, have in fact resulted in a noticeable improvement. In England inspection is still done almost entirely by sanitary inspectors holding a special certificate in meat inspection, a system which many people think should give way to one supervised by veterinary surgeons.

Emergency killings—that is to say killings done without prior notice and in unauthorized places—have always caused trouble. Figures from Germany show that three-quarters of the illnesses caused by meat infected with *Salmonella* can be traced to emergency killings, in spite of the fact that there the law requires such carcasses to be detained until they have been examined bacteriologically; in Austria no emergency slaughter is allowed at all. In several countries tuberculous meat is passed after sterilization, but this has never been legalized here, and, though some meat would be saved, it is doubtful if even to-day the British public would look favourably on such a practice. In the past British standards of judgment were severe, and much good meat, when inspected at all, was condemned unnecessarily. But during the war meat inspectors began to show greater discrimination, and there is no reason to believe that they do not still pass as much meat as is possible without risk to the public.

Meat inspection in England could be greatly improved. The Ministry of Health has for over twenty years advocated the ante-mortem inspection of animals awaiting slaughter, but few local authorities have made the necessary veterinary appointments. Ante-mortem inspection reveals many animals which are obviously sick but which may show few physical signs of disease on post-mortem inspection. Such inspection is desirable, but the routine inspection of one carcass after another is dull and monotonous work which few veterinary surgeons would care to undertake even if there were enough of them, and it might be better to appoint trained and experienced men, not necessarily sanitary inspectors, to do the routine work under the general supervision of a veterinary surgeon, as is the practice in Scotland. But such a change would not be possible unless the Government decided to restrict permanently the number of slaughter-houses. Many of them, too, need to be drastically improved. There is much to be said in favour of combining the supervision of slaughter-house inspection with the control of disease in herds, a function of the Animal Health Division of the Ministry of Agriculture.

[1] *Vet. Rec.*, 1948, **60**, 595.

THE PRODUCTION OF INSULIN

The demand for insulin continues to increase, since the number of patients who suffer from diabetes mellitus and remain alive grows larger every year and, in addition, patients with schizophrenia are now treated with insulin shock. The sole source of insulin is the pancreas obtained from cattle and fish, and reports received by WHO show that over a ten-year period there may be an annual deficit of 400,000,000 international units if production remains at the same level. In this country fortunately there appears to be no danger of shortage. Mr. J. C. Hanbury,[1] chairman of the British insulin manufacturers, has recently pointed out that "the production of insulin . . . is adequate to meet in full both home and export demands, and ample stocks are always maintained." The position in Germany, however, is not satisfactory, and great efforts have been made to improve the output. In order to obtain the best yield of insulin the pancreas glands should be cooled rapidly to a temperature of $-20°$ to $-30°$ C. This process is impracticable in the small abattoirs in Germany, and Dr. F. Lindner[2] has introduced a method of chemical dehydration. The fresh pancreas is collected as soon as possible after slaughtering, cleaned, and placed in cold storage at a temperature of 5–8° C., which is fairly easily achieved. Some time within the next twelve hours the glands (12–15 kg. at a time) are placed on the plate of a butcher's rotary cutting machine and 700 g. of finely ground anhydrous sodium sulphate added for each kilogram of pancreas. The machine is then started and in ten minutes the pancreas has been completely disintegrated and intimately mixed with the sodium sulphate. The mass is spread on iron plates in a layer 5 cm. thick for one hour and then placed in the refrigerator. The next day the slabs are hard and are stored in a refrigerator at 5–8° C. until needed, but they can be stored at room temperature, up to 30° C. if necessary, without damage. The extraction of the pancreas then proceeds in the usual way. It is stated that the yield is as good as that obtained by the freezing method, but Mr. Hanbury disagrees with this. It seems clear, however, that chemical dehydration will enable insulin to be extracted from pancreas which would otherwise be wasted and that it should help to increase the supplies of insulin in all countries in which the abattoirs have no means of freezing the fresh pancreas. Meanwhile research on the constitution of the insulin molecule continues, and success in this respect would probably soon lead to the synthetic production of insulin. Once this is achieved all anxiety about the supply of insulin should be at an end. It is to be hoped that the efforts of the chemists will soon be crowned with success.

The Milroy Lectures will be delivered by Dr. Marc Daniels, M.R.C.P., before the Royal College of Physicians of London (Pall Mall East, S.W.) on Tuesday and Thursday, Feb. 15 and 17, at 5 p.m. His subject is "Tuberculosis in Post-war Europe."

[1] *The Times*, July 23, 1948.
[2] *Chron. World Hlth Org.*, 1948, **2**, 153.

MODERN LANGUAGES IN THE SERVICE OF MEDICINE

BY

RAYMOND WHITEHEAD, M.D., D.Sc.

(From the Department of Pathology, University of Manchester)

At one time or another the problem of foreign languages presents itself to a large proportion of the medical profession. French and German are among the essential tools of the teacher and research worker, and are of at least temporary concern to the candidate for a higher degree by thesis. Other modern foreign languages are not widely cultivated by British medical men, but those who can read them are valued as translators, reviewers, and abstracters. For these reasons it is of interest to determine how far various languages are used by medical writers and to discuss the problems that the diversity of languages creates for medical libraries, readers, and authors.

Languages of Publications Indexed

Table I shows the publications indexed in the *Quarterly Cumulative Index Medicus* classified according to language.

TABLE I.—*Languages of Publications Indexed*

	Books			Journals		
	1937	1947	Changes since 1937	1937	1947	Changes since 1937
Czech	1	—	−1	6	4	−2
Danish	2	1	−1	3	3	—
Dutch	4	2	−2	7	10	+3
English	525	584	+59	417	531	+114
French	188	44	−144	197	103	−94
German	264	42	−222	176	41	−135
Hungarian	—	—	—	5	1	−4
Italian	112	122	+10	129	116	−13
Norwegian	—	—	—	2	—	−2
Polish	—	—	—	4	2	−2
Portuguese	6	13	+7	33	73	+40
Rumanian	—	—	—	7	—	−7
Russian	5	7	+2	14	14	—
Spanish	13	56	+43	85	216	+131
Swedish	1	—	−1	1	1	—
Unclassified	13	8	−5	75	44	−31
Total	1,134	879	−255	1,161	1,159	−2

The figures were calculated from lists in the *Quarterly Cumulative Index Medicus*, Vols. 21 and 41. The lists relate only to the first six months of each year.

The figures for 1937 show that the leading languages were English, French, German, and Italian; in 1947, on the other hand, they were English, French, Italian, and Spanish.

The figures for other languages for both years raise doubts about the completeness of the *Index*. For example, it is difficult to accept the suggestion of the figures that only a dozen medical books in Russian appear each year or that the medical journals in this language number no more than fourteen. The figures for Swedish—one book and one journal—are likewise almost certainly too low; the catalogue of the Swedish Publishers' Association for 1946 lists sixty-three books and twenty-one journals dealing with medical subjects in the Swedish language. These comments are made not by way of criticism of the indexers, who obviously can deal only with publications accessible to them, but to indicate that a language may be used by medical writers more extensively than the *Index* would suggest.

Three languages show substantial gains since 1937—namely, English, Spanish, and Portuguese. Table II shows the contributions of Europe and America to these gains. It also shows that each language gained in both Europe and America, but that the gains by each language were both absolutely and relatively greater in America.

TABLE II.—*Main Sources of Indexed Journals in English, Spanish, and Portuguese*

	1937	1947	Gains since 1937	
			Actual	Percentage
British Isles	91	95	4	4·4
United States	272	372	100	36·8
Spain	13	27	14	107·7
Spanish America	68	186	118	173·5
Portugal	4	8	4	100·0
Brazil	28	66	38	135·7

The figures were calculated from the lists of journals indexed in the *Quarterly Cumulative Index Medicus*, Vols. 21 and 41.

Languages of Journals in a Library

The Manchester Medical Library takes approximately a quarter of the journals indexed; Table III shows (*a*) the language distribution that would be expected if its list of journals were a miniature replica of the list of journals indexed, and (*b*) the language distribution observed.

TABLE III.—*Languages of Journals in a Library Taking a Quarter of the Journals Indexed*

	Expected			Observed		
	1937	1947	Changes since 1937	1937	1947	Changes since 1937
English	104	133	+29	197	253	+56
French	49	26	−23	28	26	−2
German	44	10	−34	46	—	−46
Italian	32	29	−3	2	—	−2
Portuguese	8	18	+10	1	—	−1
Spanish	21	54	+33	3	2	−1
Others	31	20	−11	11	4	−7
Total	289	290	+1	288	285	−3

The "expected" figures were found by dividing the figures in Table I by 4, "others" including both the "unclassified" of Table I and languages specified in Table I only. The "observed" figures were calculated from lists in the *Annual Report of the Manchester Medical Society* for 1936–7 and 1946–7.

In each year the observed figure for English is much higher than the expected; on the other hand, the observed figures for Spanish and Italian are in each year much lower than the expected.

Languages of Articles Abstracted and Books Reviewed

Table IV gives examples of the languages of (*a*) articles abstracted in *Abstracts of World Medicine*, and (*b*) books reviewed in the *British Medical Journal*.

TABLE IV.—*Languages of Articles Abstracted and Books Reviewed*

	Articles	Books		Articles	Books
Czech	1	—	Italian	25	1
Danish	5	—	Norwegian	9	—
Dutch	3	—	Polish	2	—
English	816	245	Portuguese	3	3
French	56	29	Russian	13	—
German	44	14	Spanish	10	3
Hebrew	1	—	Swedish	9	1
Hungarian	2	—	Turkish	1	—

The figures relate to the first 1,000 articles abstracted in *Abstracts of World Medicine*, 1947, Vol. 2, and to the 296 books reviewed in the *British Medical Journal* in 1947.

Of the articles abstracted, over four-fifths were in English, and the only foreign languages individually accounting for more than 2% of the total were French, German, and Italian. Of the books reviewed, over four-fifths were in English and most of the others were in French or German.

Languages and Library Policy

The importance of various languages varies with the point of view. The most general point of view is perhaps that of a library committee, whose task is to meet the needs of a medical community. One of the main functions of such a committee is the selection of journals; according to the funds and space at its disposal, it has to provide the journals that will be most useful to the readers it serves. Its work may involve making judgments of quality between journals in the same subject, or deciding between the claims of journals in different subjects. General usefulness, as well as quality, must be considered; it would be uneconomic to take a journal, however excellent, in a language that no one could read. The decision not to take a particular journal therefore does not necessarily mean that it is of poor quality; on the contrary it may be of good quality but in too small demand to justify a subscription. An unfavourable decision does not entail hardship for a reader, who can usually borrow the journal from some other library, either

direct or through his local library; alternatively he may obtain an individual article in the form of a reprint from the author or of a photostatic or microfilm copy. In reaching decisions a library committee naturally bears in mind these various possibilities.

Comparison of the "expected" and "observed" figures in Table III shows a strong preference for journals in English. This is not surprising, since English is the language most widely read by users of the library. The library serves both practitioners and the university staff. It is known that requests for journals in foreign languages are virtually confined to the university staff, and it is accordingly their judgment that is reflected in the figures for French and German. The insignificant representation of other foreign languages probably means that few if any users of the library read them; it does not mean that the medical literature in these languages is unimportant—evidence to the contrary is provided by a steady demand for translations from them by those using the library. The language from which translations are required most often is probably Italian, and on some topics the literature in this language is substantial; for example, in a study of Still's disease (Langley, 1945) no fewer than 9 out of 30 references are to Italian papers.

Selection of Articles for Abstracting

The abundance of medical literature has led to a demand for summaries or abstracts of medical articles, and there are now, of course, several journals consisting entirely of such abstracts. The reading of abstracts is a convenient means of keeping in touch with developments in medicine, but it must always be remembered that an abstract is a second-hand account, however skilfully rendered. An abstracter has to condense pages into sentences, and must inevitably select for mention the points that he himself thinks important or interesting. As a rule, his selection of points can be made only in the light of his general experience; even if he happens to be an expert on the subject of an article, other experts might dissent from his judgment. Anyone working on a particular topic must consult an article in the original (or in translation) and form his own opinion of its value; all that he needs is a list of titles of articles such as those given in the *Index Medicus*. When all efforts to obtain access to an article have failed it is permissible to quote an abstract in the list of references at the end of a paper; such a quotation can properly be made only for information, for it would not be fair to an author to judge his work on the evidence of an abstract.

Because of their limited value, abstracts are costly. Their cost is to be measured less by the price of abstract journals than by the diversion from other work of the energies of abstracters, who are themselves often engaged in research. The preparation of abstracts is an exacting task and a severe test of critical and literary powers combined; if the text is in a foreign language great care is needed to avoid mistranslations. For these reasons the selection of articles for abstracting is a heavy responsibility, and the aim should be to provide the best possible service with the minimum expenditure of effort. Ideally, articles should be chosen for their quality or interest irrespective of the language in which they are written, but in practice the choice may fall short of the ideal owing to inaccessibility of journals or lack of linguists. The example in Table IV certainly suggests a preference for articles in English, but the best articles may in fact have been in English, in which case it would not necessarily represent a departure from the ideal policy.

Because of the widespread knowledge of English and the ready accessibility of journals in English, it might be suggested that articles in English do not need abstracting, and that abstract journals would be more useful if they confined themselves exclusively to abstracts of articles in foreign languages. Such a policy would undoubtedly have the advantage of disseminating information that would otherwise remain relatively inaccessible, but it is doubtful whether most users of abstracts would be willing to forgo the convenience of having a balanced review of the whole of current medical literature.

Selection of Books for Review

The restriction imposed by general ignorance of foreign languages is more severe for book reviews than for abstracts and of the same nature as that influencing the selection of journals by a library. The abstracter is free to range widely in the literature in foreign languages, for many of his readers will be content with his abstracts and not read the original articles. The book reviewer, on the other hand, is largely concerned with introducing books to potential readers. Book reviews would therefore be expected to deal mainly with books in the mother tongue, and the range of foreign languages providing books reviewed would be expected to be narrower than for articles abstracted. The data in Table IV are therefore in agreement with expectation.

The Englishman already has access to a large amount of foreign literature in his own language; for English is of course the mother tongue of many foreign countries, the United States being simply first among them. At the same time the close genetic relation between medicine in the British Isles and medicine in the other English-speaking countries gives the medical literature of these countries a special interest for the Englishman, and the books they publish are often of more immediate use to him than those from countries speaking foreign languages. Books in foreign languages—especially textbooks—often reflect practice that differs considerably from that in the English-speaking countries; for this reason they are in general less interesting than books in English, and reviews are accordingly less necessary. There are of course notable exceptions, and it is most desirable that they should be reviewed; in this matter we must look to the enterprise of foreign publishers and foreign cultural representatives in this country in submitting books for examination.

Reviews for journals published in this country should preferably be written by natives of the British Isles, since the value of such reviews largely depends on their being written against the background of our own system of medical education and practice; a review of a foreign book (whether in English or some other language) by one of the author's fellow-countrymen could hardly carry the same weight. The medical profession in this country is large enough to provide reviewers of books in every important European language, and medical men with linguistic ability should be aware of this opportunity of serving their colleagues.

Languages and the Individual Reader

Medical men who have to read articles in foreign languages are mainly specialists, and therefore interested not so much in the total output in any language as in the leading journals in their own subjects. For any individual this probably means one or two journals in each of a considerable number of languages; if he cannot read a language he must have articles translated. The languages most frequently needed are French and German; anyone who has learnt both at school has thus saved himself much time and trouble. On this subject we could hardly improve on the observations of La Bruyère (quoted by Locke, 1692):

> "One can scarce burden Children too much with the Knowledge of Languages. They are useful to Men of all Conditions, and they equally open them the Entrance, either to the most profound, or the more easy and entertaining Parts of Learning. If this irksome Study be put off to a little more advanced Age, young Men either have not Resolution enough to apply it out of Choice or Steadiness to carry it on. And if any one has the Gift of Perseverance, it is not without the Inconvenience of spending that Time upon Languages, which is destined to other Uses: And he confines to the Study of Words that Age of his Life that is above it, and requires Things; at least it is the losing the best and beautifullest Season of one's Life. This large Foundation of Languages cannot be well laid but when every thing makes an easy and deep Impression on the Mind; when the Memory is fresh, ready and tenacious; when the Head and Heart are as yet free from Cares, Passions, and Designs; and those on whom the Child depends have Authority enough to keep him close to a long continued Application. I am persuaded that the small number of truly Learned, and the Multitude of superficial Pretenders, is owing to the neglect of this."

French usually presents no problem, for it is commonly learnt at school and can be quickly revised if necessary; German, on the other hand, is less often studied at school and is generally considered to be the more difficult language. German is important owing to the large amount of good work

published in it before the war and will retain its value for years even if there is no revival in German medicine.

Whether any further language should be acquired is a matter for the individual to decide. The learning of French and German, especially if either has to be learnt after leaving school, may well take up all the time that can be spared for language studies, and only those with a special interest in languages are likely to proceed further. Those who do so will find that English and German together smooth the way to the other Germanic languages; Icelandic is highly inflected and at least as difficult as German, but the other important members of this group—Danish, Norwegian, Swedish, and Dutch—are all grammatically simpler than German and among the easiest of foreign languages for the Englishman. French is similarly helpful in the study of Italian, Spanish, Portuguese, and Rumanian, all five being descendants of Latin.

Tables I and IV together show that medical literature is published in fourteen foreign languages other than French and German, and the lists are almost certainly incomplete; the medical linguist thus has a wide choice, and the selection for study of a foreign language other than French and German may rightly be influenced by non-medical interests such as general literature or foreign travel. The medical reader of any foreign language other than French and German will probably attract as much work as he can comfortably cope with, and if he teaches in a university he may expect work from colleagues in any faculty.

Languages from an Author's Standpoint

The language problem for a medical author is relatively simple, for the choice lies between his mother tongue and one or other of the so-called world languages—English, French, and German—if he was not born into one of these. The advantages of writing in one's native language need no discussion, for no one can feel quite so much at home in any other; an Englishman would be the last to question an author's right to publish in his own language if he so desires. On the other hand, the disadvantages—namely, a limited public and the risk of being misunderstood by foreign readers—are equally obvious, and with many writers outweigh the advantages. Such writers vary in their choice of language, which is often determined by the traditional intellectual relations of their countries; thus German is often used by Russians and Japanese, and French by citizens of the other Latin countries. English ensures the widest public, and foremost among those who use it are the Scandinavians. Let us be grateful for their choice and hope that their example may be followed ever more widely.

Summary

Publications listed in the *Quarterly Cumulative Index Medicus* have been classified according to language. In 1937 the leading languages were English, French, German, and Italian; in 1947 they were English, French, Italian, and Spanish. English, Spanish, and Portuguese show substantial gains since 1937; each language gained in both Europe and America, but the gains by each language were both absolutely and relatively greater in America. In 1947 about one-half the indexed journals were in English and about one-fifth in Spanish; no other language accounted for more than one-tenth.

Comparison of indexed publications with (*a*) journals in a library, (*b*) articles abstracted, and (*c*) books reviewed shows a strong preference for journals, articles, and books in English; the implications of this preference are discussed.

The value of French and German, both as keys to medical literature and as aids to the study of other languages, is emphasized. The data show that medical literature is published in at least fourteen foreign languages other than French and German, and it is suggested that the selection for study of foreign languages other than French and German may rightly be influenced by non-medical interests. The advantages of publishing in world languages, especially English, are noted.

I am indebted to Mr. G. Wilson (Librarian) and to Mr. F. C. Hirst (Cataloguer), of the Manchester Medical Library, and to Professor S. L. Baker for their kindness in reading the manuscript.

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ORDER OF ST. JOHN OF JERUSALEM

The *London Gazette* has announced the following promotions in, and appointments to, the Venerable Order of the Hospital of St. John of Jerusalem:

As Knight: Dr. C. E. C. Wilson. *As Associate Knights:* Major-General K. S. Master, M.C., K.H.P., and Dr. Jivraj N. Mehta. *As Dame:* Dr. Margaret E. Douglass. *As Commanders (Brothers):* Brigadier R. A. Hepple, C.B.E., M.C., M.B., Colonel C. P. Gaboury, O.B.E., M.D., Major E. S. B. Hamilton, M.C., F.R.C.S., Drs. C. A. Verco and C. Thompson. *As Commander (Sister):* Lady Isabel E. Hutton, C.B.E., M.D. *As Officers (Brothers):* Brigadier F. A. E. Crew, M.D., Colonel M. MacEwan, D.S.O., O.B.E., D.F.C., T.D., M.B., Lieutenant-Colonels D. W. C. Gawne, M.D., F.R.C.S., R.A.M.C., H. F. Summons, M.B.E., M.B., G. N. Morris, F.R.C.S., Majors T. D. W. Fryer, M.B., C. D. Donald, M.B., Captain S. A. Nield-Faulkner, L.R.C.P.&S., Drs. I. H. Beattie, R. I. Hyder, G. A. Macdonald, J. T. Whitley, O.B.E., H. R. Mustard, E. W. Lonsdale-White, H. M. Ayres, A. Tabone, and A. W. Azzopardi. *As Associate Officers (Brothers):* Rai Bahadur Captain K. S. Roy, M.B., and Dr. G. S. Vazkar. *As Officer (Sister):* Dr. Dora E. Wheeler. *As Serving Brothers:* Lieutenant-Colonel O. L. Appleton, T.D., L.R.C.P.&S., R.A.M.C., Major M. J. Bett, M.D., Captains F. R. Wilson, M.D., R.A.M.C., J. B. W. Meredith, M.B., F. E. Barclay, M.B., Surgeon Captain V. F. Walsh, L.R.C.P.&S., R.N., Drs. E. Sorabjee, J. G. Morgan, G. K. Arthur, J. F. E. Burns, W. J. Collins, C. E. Mathieson, D. S. Smith, H. T. H. Dimitriou, R. A. Simpson, R. B. Hick, L. W. Bradshaw, W. S. Coutts, A. W. Ewing, G. E. Sawdon, F. R. Mutch, N. Wilson, T. D. Thorne, H. F. Sparling, M.B.E., J. M. Hain, G. R. Bourne, F. W. Gershaw, H. C. Powell, G. Saine, H. M. S. Tait, A. Parkinson, F. G. Percival, O.B.E., and V. C. F. Tet. *As Associate Serving Brothers*: Drs. E. A. Leviseur and C. K. Khey. *As Serving Sisters:* Drs. Phyllis Burns, Mary E. Rolston, and Ellice E. P. Dart.

Reports of Societies

LONDON COUNTY MEDICAL SOCIETY

Addressing the London County Medical Society at a meeting held at Furnival House, Highgate, on Jan. 5, and presided over by Dr. C. D. Coyle, Mr. J. R. M. WHIGHAM, the retiring president, said that the ideal hospital had yet to be built. Design must have some relation to function, and "job efficiency" had always to be kept in mind. Nowhere in the hospital was this more necessary than in the ward. The subdivided ward, with opportunities for recreation for those able to enjoy it, was an urgent need for the future.

For the doctor hospital medicine was not total medicine, and every opportunity should be taken to fill in the gaps so that the patient could be studied in the light of his family, his house, his job, and his pay. Close contact with the relatives was desirable, and on transference back of the patient the general practitioner should be given a full account of the case.

Though the doctor was not immediately concerned with rising hospital costs he could by careful scrutiny see that the maximum use was made of the beds of which he was in charge. The aged sick who were acutely ill, and those likely to benefit by it, should receive hospital treatment. Others should be kept at home, and no one wanted this more than the elderly patients themselves. Unfortunately some homes were not only not fit to live in, they were not even fit to die in. The hospital had to rescue these unfortunate people. It was not realized, either inside the profession or outside, how numerous were the day-to-day administrative problems in a hospital dealing with all sorts and conditions of patients. The need for "a head" remained, and, a hospital being what it was—a medical service primarily—that head was most naturally a doctor. Medicine to be at its best must flow freely and naturally and not be forced along artificial channels. No two hospitals were alike; each had its own problems, and therefore must be allowed some degree of autonomy.

SCOTTISH SURGICAL PAEDIATRIC CLUB

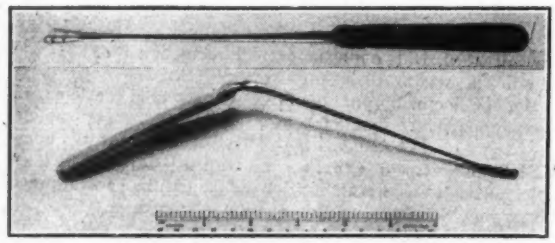
In view of the increasing number of surgeons whose work is wholly or mainly concerned with infants and children, a Scottish Surgical Paediatric Club has been formed. The first meeting was held in Glasgow and was attended by twenty-seven members, representing Aberdeen, Dundee, Edinburgh, Glasgow, and Inverness. A dinner was held in the Royal Faculty of Physicians and Surgeons on the evening of Dec. 17. On Dec. 18 a very full day was spent at the Royal Hospital for Sick Children, Glasgow. Four short papers were read in the morning, and the afternoon was devoted to clinical and pathological demonstrations. The next meeting will be held in Aberdeen in May.

Preparations and Appliances

ENDOMETRIAL BIOPSY CURETTE

Dr. ERNST FRIEDMANN, Fertility Department, Royal Free Hospital, writes: The importance of endometrial studies in functional sterility and long-standing amenorrhoea has long been recognized. The number of instruments which have been recommended for endometrial biopsies shows that none has really proved satisfactory, whether it be endometrial punch forceps, the intrauterine suction apparatus, the suction cannula with syringe, or models like Sharman's curette, the disadvantage of which seems to be the "dead space" in it.

I have therefore designed a curette which can readily be used on out-patients without danger and with the least discomfort. The total length of this curette is 10½ in. (26.5 cm.). It has a flat handle with a groove at the distal end to allow a comfortable but firm grip. The stem is graduated, is malleable, and terminates in an inverted V-shaped loop, in which are incorporated two cross-bars which play an important part—i.e., retain the specimen. The calibre corresponds to the thickness of an ordinary uterine sound, which in my opinion should always be passed before introducing the curette. The cervix should be steadied with a vulsellum. The curette is then drawn down the upper part of either the anterior or the posterior wall or both with slight pressure only and without undue force. On immersing the curette in the fixing solution the piece comes off readily. Only occasionally have I found it necessary to shake the curette a little.



I have used this curette exclusively since 1946 in 300 biopsies. In all but those very few cases in which a uterine sound could not be passed and consequently the curette could not be inserted the strip of endometrium was such that glands and stroma were not separated or fragmented. It was almost always a single strip which on section included practically the length of the glands with surface epithelium and stroma intact.

The instrument is manufactured by Allen and Hanburys Ltd. in stainless steel, and is available with straight or angled handle.

Edward A. Humphreys, M.D., of Columbus, Ohio, U.S.A., has been appointed President of the American Association on Mental Deficiency. Dr. Humphreys qualified in 1930; after working in the New York Psychiatric Institute and the Fifth Avenue Hospital he was for ten years Director of Research at Letchworth Village. In 1945 he assumed his present post as Chief of the Bureau of Prevention and Education, Division of Mental Hygiene, Ohio, and has served as Acting Commissioner of Mental Hygiene for over a year.

Correspondence

Significance of Proteins in Nutrition

SIR,—Readers are supposed to serve some sort of useful service by calling attention to errors which they have detected and by making comments which may be of some interest to other readers. I hesitate to make these adverse criticisms of an otherwise excellent paper by Dr. D. P. Cuthbertson (Oct. 23, 1948, p. 731) on the significance of proteins in nutrition and their particular importance during convalescence.

1. The author at one point states, "Satisfactory nutritional preparations will undoubtedly extend the benefits of surgery," and includes in these "high-protein, high-carbohydrate diet fed where necessary by tubal methods"; yet elsewhere the contradictory statement is made, "There is little point in trying to supply the patient with food in excess of that which appetite dictates." It has become abundantly clear to me on the basis of many personal observations that nutritional depletion occurs in many surgical patients because the surgeon fails to combat anorexia. That Dr. Cuthbertson has failed to emphasize this important point is illustrated by a letter in your *Journal* (Nov. 27, 1948, p. 959) from Dr. E. Sakochansky, who quotes the Cuthbertson paper to justify reliance on the patient's appetite, saying, "Much needless anxiety would be removed thereby," and casting aspersions upon the feeling of relatives who "are apt to worry unduly because a sick person does not eat."

2. In deprecating the use of intravenous amino-acid mixtures Dr. Cuthbertson states, "Plasma and glucose are safer fluids," which is a little misleading inasmuch as these two substances can scarcely be compared on the basis of commonly observed potential reactions.

3. Spence, Evans, and Forbes (*Ann. Surg.*, 1946, **124**, 131) are quoted as having made a study of a mixture of ten essential amino-acids (including their intravenous use), whereas these workers actually employed oral preparations of whole protein in their surgical cases.

4. Dr. Cuthbertson quotes a paper of mine incorrectly by stating that "90 g. of protein takes 8 to 9 hours in a volume of 2,500 ml." Actually, in my experience with thousands of injections 50 g. of amino-acid mixtures rarely require more than 3 hours, and this is given in a volume of 1,000 ml. Our routine is to give an average-sized adult patient unable to eat two litres per day, one in the morning and one in the afternoon, each requiring between 2 and 3 hours for the intravenous injection. Each litre contains 50 g. of amino-acid mixture and 50 g. of glucose, plus a little over 2 g. of sodium chloride.—I am, etc.,

Saint Louis, Minnesota. ROBERT ELMAN.

SIR,—Dr. Robert Elman was good enough to send me a copy of his letter (see above), and I should like to consider it paragraph by paragraph.

1. My statement that "satisfactory nutritional preparation will undoubtedly extend the benefits of surgery," including "high-protein, high-carbohydrate diet fed where necessary by tubal methods," refers to pre-operative treatment of depleted patients, when it is desirable to secure as much restitution as possible of body tissue by ingested or infused food material. When I make the statement, "There is little point in trying to supply the patient with food in excess of that which appetite dictates," I am referring to the immediate phase of protein catabolism following injury, when I consider that the body is not, in general, geared to anabolic activity. I had hoped that both these points were made clear in my paper.

2. Dr. Elman will find my most recent views on protein hydrolysates and pure amino-acid mixtures in my paper on "Assessment of Knowledge Concerning the Clinical Use of Protein Hydrolysates and Pure Amino-acid Mixtures" (*Amer. J. Med.*, 1948, **5**, 879), which I was invited to contribute as the concluding paper to a series of seminars on protein hydrolysates and pure amino-acid mixtures presented by a group of experts including Dr. Elman.

3 and 4. I freely admit being in error over the reference to the paper by Spence, Evans, and Forbes, and to the one by Dr. Elman. The work referred to in both cases is that by S. C. Werner (*Ann. Surg.*, 1947, **126**, 169). On looking over my earlier notes I find that by some mischance the references became misplaced, though on again reading Werner's paper (para. 1) it does seem as if he is quoting Dr. Elman when he states, "To administer the equivalent of 90 g. of protein requires eight or nine hours and a volume of 2,500 ml."

I am grateful to Dr. Elman for pointing out these errors in my references.—I am, etc.,

Bucksburn, Aberdeenshire. D. P. CUTHBERTSON.

Resistant Staphylococci

SIR,—The annotation entitled "Resistant Staphylococci" (Jan. 8, p. 64) raises the interesting and important question how much the bacteriologist can help the clinician in deciding the probable effect of penicillin in a particular case of infection due to a penicillinase-producing strain of *Staph. aureus*. The important question for the clinician is not how much penicillinase can be artificially extracted from a given organism, but whether the organism can produce the enzyme in sufficient quantity and quickly enough to permit it to grow in concentrations of penicillin obtainable in the human body. The double sensitivity test, using two different-sized inocula, is probably the most informative, and, as pointed out by Gilson and Parker,[1] the difference is directly related to penicillinase production. Investigations of this type on 18 penicillinase-producing staphylococci recently isolated from cases of infection in this hospital gave the following results:

Greatest Concentration of Penicillin permitting Growth		No. of Strains
Large Inoculum (Approx. 1,000,000 Organisms)	Small Inoculum (Approx. 1,000 Organisms)	
50 or more u./ml.	1–4 u./ml.	7
50 or more u./ml.	0·25–0·5 u./ml.	5
25 u./ml.	1 u./ml.	1
25 u./ml.	0·25–0·5 u./ml.	2
12·5 u./ml.	0·25 u./ml.	1
12·5 u./ml.	0·03 u./ml.	1
1·0 u./ml.	0·13 u./ml.	1

It seems probable from these results that some of the strains would respond more readily to penicillin treatment than others, but there are still at least three unknown factors. First, what is the number of organisms penicillin is likely to encounter in a given infection? Secondly, do staphylococci produce penicillinase at the same rate *in vivo* as *in vitro*? And thirdly, does an organism which only produces small quantities of penicillinase acquire the ability to produce more in the presence of small quantities of penicillin?—I am, etc.,

St. Thomas's Hospital, London, S.E.1. MARY BARBER.

REFERENCE

1 *J. Bact.*, 1948, **55**, 801.

Pensions for Diabetics

SIR,—My letter (Nov. 13, 1948, p. 875) has aroused many letters of criticism from many angles. It is impossible to deal with all, but I should stress again some facts that made me write the letter.

(1) The Army Pensions Board seems to be very generous in awarding pensions to diabetics in cases of grave hardships in the Services after which diabetes has soon followed. But the great majority of appellant cases referred to me arise in circumstances comparable with, or even less straining than, those of civilian life, certainly less tense and difficult than wartime London. If all persons developing diabetes outside the Services under comparable conditions were to be pensioned, well and good perhaps. But merely to deserve a pension because diabetes develops while on war or post-war service is the position which I criticize in relation to pension awards.

(2) It should not be forgotten that the recognition of diabetes as a pensionable disability contradicts a status of ordinary working health and capacity which most diabetics cherish. They want to be, and are, capable of housewifery and other full employment, except in some quite unsuitable jobs. They want to be accepted for superannuation and limited life assurance and not to be shut out from the posts that twenty-five years of insulin have proved the majority to fill normally for many a year.

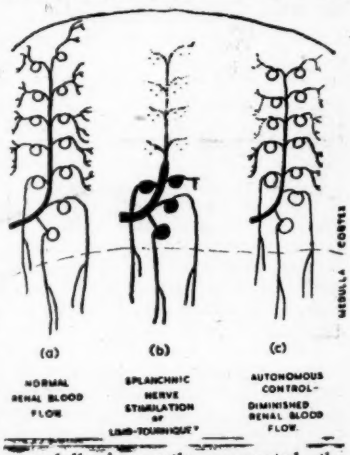
I have been accused of being "unsympathetic" and "hard-hearted" to diabetics in my written attitude about pensions, and this rather hurts me. I was solaced last week to receive an unexpected letter from Dr. Elliot P. Joslin, of Boston, Mass., who has done more than anyone else in the world for diabetics' interests for fifty years. He wrote to say he supported my attitude towards pensions "one hundred per cent." But I could never be 100% certain of any point of view I formed on diabetes, although this is what the legal attitude asks one to be.—I am, etc.,

London, W.1. R. D. LAWRENCE.

Anuria

SIR,—Permit me to correct a misstatement which appears in the paper by Drs. D. A. K. Black and S. W. Stanbury on the treatment of anuria (Dec. 25, 1948, p. 1101) and in your leading article on that subject in the same issue (p. 1111). Drs. Trueta and Barclay and their colleagues did not demonstrate, neither did they describe, a *shunt* in the renal circulation. They showed that in the rabbit the application of a tourniquet to a hind limb for some hours, or the stimulation of (1) the central end of the cut sciatic nerve or (2) the distal end of the cut splanchnic nerve, resulted in a short-circuiting or a diversion, or, more correctly stated, an alteration, of the blood-flow through the renal cortex, so that the greater volume, practically the whole of the blood, subsequently flowed through the medulla (at increased rate), while the amount flowing through the outer- and mid-cortex was so far reduced as to fail to show radiographically.

The recent misstatements have arisen, probably, chiefly from a lack of understanding of the anatomy of the renal circulation, and it is well that correction be made now before these misstatements are referred to or repeated elsewhere. The renal circulation is primarily glomerular[1] and is shown as (*a*) in the accompanying diagram: all the glomeruli are situated in the cortex, and the blood which flows through the great majority (about 85%) traverses the peritubular capillary plexuses of the cortex. The blood which flows through the most proximal glomeruli, those of the boundary zone (about 15%), passes to the medulla, whose normal (and sole) blood supply it is—hence the name juxtamedullary which I gave to these proximal glomeruli in 1941.[2]



When a limb tourniquet is applied, or the central end of the cut sciatic or the splanchnic nerve is stimulated, vasoconstriction in the renal arteries brings about greatest reduction in the calibre of the cortical (intralobular) arteries, so that the circulation in the outer- and mid-cortical glomeruli (*circa* 80%) appears to cease, while as a consequence the circulation through the juxtamedullary (15%) and some (5%) deep cortical glomeruli and the medulla is greatly augmented, the juxtamedullary glomerular capillary loop-velocity much increased and the renal circuit-time reduced by half (see (*b*) in the diagram).[3 4 5]

In the group of conditions in which lower nephron damage is a common feature—blackwater fever, crush syndrome, incompatible blood transfusion, concealed accidental haemorrhage in pregnancy, excessive vomiting in pyloric stenosis, cholera, and yellow fever—it is most probable that the extreme reflex vasoconstriction of cortical vessels (above mentioned) does not occur, but rather is the partial renal cortical ischaemia due to an exaggeration of the normal autonomous control in the kidney by which the intrarenal blood flow is adjusted to the varied conditions of the general circulation. In discussing the

pathogenesis of the renal failure in the three conditions first mentioned Foy and his colleagues[6] drew attention to the dehydration in such patients, and they concluded that the anuria is associated with the diminution of blood volume, of renal blood flow, and of glomerular filtration. It seems reasonable, therefore, to conclude that in respect of the reduced renal blood flow in these conditions the degree and duration of cortical ischaemia are determined by the autonomous control of the kidney which increases the tone of the renal arteries (in endeavour to maintain the renal blood flow in the face of reduced blood volume), producing proportionately greater vasoconstriction in the intralobular arteries, so that there is partial ischaemia in the outer cortex—(*c*) in the diagram. Anaemic anoxaemia from external or internal blood loss and pigment athrocytosis from haemoglobinuria or myohaemoglobinuria are to be regarded as additional factors in the pathogenesis of the tubular lesion and renal failure. Similar views are stated more fully in a leading article in the *Lancet*,[7] and simple statement only need be made here to outline the intrarenal circulatory changes.

As regards true vascular shunts in the renal circulation such as those described by Steinach,[8] Spanner,[9] Trueta and his colleagues,[5] and Simkin,[10] the precise nature, number, and function of these are not yet fully understood.—I am, etc.,

London, N.18. J. F. HEGGIE.

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Whither Tuberculosis?

SIR,—The letters from the pens of Drs. G. Lissant Cox (Dec. 25, 1948, p. 1118) and Stephen Hall (Jan. 8, p. 70) are valuable contributions to a survey of the present situation. Volumes might be written on "Whither Tuberculosis?" But may I take up a little of your space?

Everyone to-day has to try to encompass too much, and this in spite of specialization and the splitting up of medical practice. Again, procrastination and delay are too common because of the shortage of beds, nurses, and, to some extent, of properly trained doctors and their valuable and numerous assistants. These things are largely due to post-war conditions and to the haste, uncertainty, and incompleteness of present changes. Delay leads generally to the disadvantage of the patient.

The desire of sanatorium physicians to share in the work of the clinic and to study environmental factors is laudable: enlarging the vision and widening the interests are healthy desires. But sanatorium doctors must realize it is a whole-time job to look after the treatment of the patients under their care. To make a complete diagnosis of the whole position is a first requisite of good treatment. In so far as this may necessitate a delving into causal factors, physical and mental, it may involve a study of sociological conditions and much else.

But the first duty of the sanatorium physician is to master all the details in the treatment. For example, an artificial pneumothorax is not a simple form of treatment, as Dr. Hall has pointed out. The complications which arise in its course are lessened and the end results improved according to the skill, experience, and clinical instinct of the managing physician; and this depends even more upon his competence in carrying the treatment along and through than upon his judgment on the choice of the patients for this particular form of collapse therapy. Furthermore, apart from the necessity of keeping abreast of the developments of thoracic surgery in order to use his acumen as a physician in supervising what to do and when to do it, the introduction of specific drugs and a closer supervision of the early stages of the rehabilitation of the patient all keep the sanatorium physician busier than ever. Perhaps the day has gone by when men of the stamp of Peter Edwards—to name only one—can make valuable contributions to many branches of the combating of tuberculosis.

So again I say, no longer can we repeat, as once was done, that prevention and cure go hand in hand. Whatever can be said about prevention and treatment going together in theory, in practice to-day they must be separated (*pace* Dr. Lissant Cox), otherwise "many will overlap and wrestle with too many details." By the way, I can make out neither head nor tail of one of Dr. Lissant Cox's sentences—"Tuberculosis, environmental and clinical, now merges into a general medical directive." This is a bit of new jargon to me. And I am a little puzzled by his, "If the new chest physician . . . exalts diagnosis and treatment and ignores prevention, he may gain entry into the . . . portals of general medicine but will have lost his soul." I would like every chest physician to "have his feet on the ground" in general medicine before he ever specializes.

It seems to me that the ways of collaboration between the chest physician and his colleagues in various other spheres are complicated and have by no means been worked out yet.—I am, etc.,

Mundesley, Norfolk. S. VERE PEARSON.

SIR,—The letters of Dr. G. Lissant Cox (Dec. 25, 1948, p. 1118) and Dr. Stephen Hall (Jan. 8, p. 70) express some of the anxieties that are troubling many of us who are employed in the tuberculosis service. Both are worried by the apparent disintegration that is taking place at many levels and in certain aspects of the service. Some of the troubles are administrative and are the result of the National Health Service Act. One hopes that with advocates such as Dr. Lissant Cox and Dr. Stephen Hall to guide our destinies many of these difficulties will be overcome in the not too distant future.

Another change about which they are both concerned is the drift of the tuberculosis officer away from social and preventive medicine to "clinical" medicine; this is surely a symptom of our nursing shortage—hence shortage of beds for the assessment and treatment of the patient's disease. The tuberculosis officer is forced to use the bed available in the patient's home and his relatives to do the nursing. With an inevitable wait of six months before "active" treatment can be started in hospital or sanatorium he is greatly tempted to do something for his patient. Through no fault of his he has entered the field of treatment, a time-consuming business, and at the expense of his other functions.

Little has been said about the training for this specialty; the success or failure of the service depends on the medical men it attracts. Rightly the emphasis in undergraduate training is on diagnosis, but it is still the practice to teach this at the bedside rather than at the chest clinic. Most postgraduate courses (Wales excepted) are held at sanatoria or university centres: why not the chest clinic or out-patient department?

The undergraduate has little time in his curriculum for social medicine; this he must learn later in general practice or some special centre. Advertisements for tuberculosis officers not uncommonly require a candidate to have a higher degree in clinical medicine: experience in general practice or social or preventive medicine is seldom asked for. It is possibly better that the potential chest physician should not be recruited from the medical officer of health's department, but it is equally unwise that his sole experience in tuberculosis should be gained treating the disease in hospital while working for higher degrees. If plans are being laid for the training of specialists in tuberculosis it is very necessary that experience in all branches of the specialty should be included if one is to stop this drift to "clinical" medicine which your correspondents foresee.—I am, etc.,

Isleworth, Middlesex. CHARLES J. STEWART.

SIR,—The letters of Dr. G. Lissant Cox (Dec. 25, 1948, p. 1118) and Dr. Stephen Hall (Jan. 8, p. 70) express a general anxiety felt at the moment by many workers in the old tuberculosis service. The necessity for a sustained campaign against the disease, using every possible method of control, direct or indirect, is so obvious to those with practical experience of the problem that any development which might appear to threaten it is naturally suspect.

This suspicion should not be interpreted as an indication that the tuberculosis service was regarded as perfect by those who worked in it. Far from it: the greater part of constructive

criticism over the last few years has in fact come from the service itself. The increasing complexity of diagnosis, the development of certain aspects of therapy in the dispensaries, and the ever-increasing numbers of cases of all kinds referred to them were recognized as a new responsibility requiring improved facilities, experienced staff, and a closer contact with other branches of medicine. Much has already been achieved, and the natural step now is to establish the modern type of clinic as a special hospital department like any other, with attached beds for diagnosis and assessment and treatment for "short-term" and emergency cases as may be appropriate.

It has also been suggested, and this is what Dr. Hall particularly questions, that the chest physician should have control of sanatorium beds, on the grounds that his experience of his specialty should be complete and a better continuity of control of the individual case established. This arrangement may or may not come about; there are arguments on both sides and it may in the end be found appropriate to one set of circumstances and not to another. Yet even without it there is certain to be an over-all increase in clinical responsibility on the part of the tuberculosis physician. It is thought that this may result in a diminished interest in the environmental and preventive aspects of the problem and that the conception of a really comprehensive tuberculosis service will be more difficult to maintain.

To add to the anxiety on this point, the responsibility for environmental and preventive work, rehabilitation, financial aid, and so on has been placed with other authorities, a matter already widely commented upon as introducing a distinct cleavage in what should be a single entity. Altogether there is need to watch developments very closely lest the attempt to meet well-recognized defects should result in the creation of new ones.

The new facilities made possible by the legislation of recent years must, however, be used to the full. Several important points come to mind, but there are two which if recognized will do much to achieve the desired end. First, the local area clinic must be regarded as the centre for the direction of anti-tuberculosis measures as a whole, and its medical staff permitted to exert a guiding influence over any outside organization concerned with the welfare of the individual patient or with the problem generally. Only in this way can the activities of the various authorities concerned be knit together into an effective comprehensive effort. Secondly, the training of staff for the senior specialist appointments must be thorough. There is a tendency in some quarters to regard a basic training in general medicine and in chest medicine as sufficient. This should certainly be the foundation, but it is not enough. Experience in sanatorium and in the chest clinics is the only way to obtain a true insight into the special characteristics of the disease and a clear understanding of the importance of epidemiological and environmental factors. Such experience should precede the appointment to a senior post. This would go far to ensure that the problem would be dealt with as a whole, without any particular aspect of it being neglected.

Finally, the multiplicity of authorities now involved will inevitably make administration difficult and complex. Auxiliary staff to deal with the detail of administration and the social side of the work must be adequate, and unless everyone appreciates the fact that the system is merely a means to an end the whole scheme will suffer. This is of the first importance in dealing with such a complicated problem as the control of tuberculosis.—I am, etc.,

Theydon Bois, Essex. HUGH RAMSAY.

Anaesthesia in Ludwig's Angina

SIR,—Dr. John H. Willis (Jan. 1, p. 31) raises the question of anaesthesia in operations undertaken for the relief of acute inflammatory conditions in the neck. As he implies in his letter, the problems involved are not universally recognized even to-day. Chevalier Jackson stated that he considered the cause of death in many cases of Ludwig's angina to be respiratory failure as a result of the administration of sedative drugs. He based this conviction on the fact that many patients sent to him suffering from this condition were either moribund or dead on arrival, although they had started their journeys as healthy persons apart from the local condition; in all cases the common factor was the administration of morphine or other sedative by well-intentioned practitioners in order to render the patients comfortable for the journey to Jackson's clinic.

The explanation of the sequence of events is clearly described by Macintosh and Bannister.[1] Briefly it is that the conscious patient is able to compensate for the early stages of respiratory obstruction by using his accessory respiratory muscles. As long as this extra thoracic effort maintains the alveolar oxygen tension at a sufficient level the patient will remain conscious. If, however, the condition is not relieved, the accessory respiratory muscles will become fatigued. Alternatively, the administration of a sedative drug will depress the respiratory centre, with consequent diminution in respiratory muscular efficiency. In either case the result is the same: the alveolar oxygen tension falls, the vital centres become anoxic, and the patient quietly stops breathing—usually without even developing laryngeal spasm.

All agents which produce unconsciousness are to a greater or lesser degree respiratory depressants at some stage in their action, and it therefore follows that to induce unconsciousness as a preliminary to surgical intervention in cases of Ludwig's angina is to court disaster. The three agents named by Dr. Willis—"pentothal," cyclopropane, and chloroform—are all potent respiratory depressants and are in my opinion contra-indicated as inducing agents in the type of case under discussion unless a certain preliminary step is taken.

The rational preliminary approach to anaesthesia in cases of respiratory obstruction resulting from Ludwig's angina, carcinoma of the thyroid, and injuries involving the upper respiratory tract is either to perform a tracheotomy under local analgesia or to pass an endotracheal tube after "cocainizing" the larynx. This latter procedure is easily accomplished with the aid of a Macintosh or a Kenton spray. Kuhn's observation[2] that laryngeal intubation enables the surgeon to become and remain master of the field is probably never better exemplified than in this method of anaesthetizing such cases of respiratory obstruction, for when the field has been mastered by laryngeal or tracheal intubation any general anaesthetic agent may safely be used, according to the indications present, to induce unconsciousness and enable the surgeon to relieve the pathological condition.—I am, etc.,

Bristol. V. TORRY BAXTER.

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SIR,—Dr. John H. Willis (Jan. 1, p. 31) comments upon the danger of using intravenous anaesthesia for the incision of acute inflammatory swellings of the neck, and I would like to carry the question one stage further back. Surely no "resident" (and here I use the term to refer to a man within a year or so of qualifying) should be expected to undertake the responsibility of anaesthetizing a patient with Ludwig's angina; the operation is rarely so urgent a matter that an experienced anaesthetist cannot be obtained.

Some residents seem frequently to be asked (or told) to give anaesthetics to dangerously ill emergency cases. I recall a well-known anaesthetist who was asked what advice he would give to a resident who had to deal with an acute intestinal obstruction; and his significant reply was, "He shouldn't: it's a specialist's job."

A "post-operative chest" following a simple herniotomy or other cold case may be regarded as a disgrace by some, but it appears that in some circles such a complication is looked upon almost as the rule after a serious upper abdominal emergency operation. Such complacency is tragic, especially when this added condition may well tip the balance fatally for the patient. So grave a responsibility surely should not rest on the shoulders of a junior but of a specialist.—I am, etc.,

Epping, Essex. ERIC K. GARDNER.

Spinal Anaesthesia for Caesarean Section

SIR,—We feel that the statements of Mr. D. Stanley-Jones (Dec. 25, 1948, p. 1121) on this subject cannot be allowed to go unchallenged. It is true that there have been cases of collapse during caesarean section under spinal anaesthesia, both reported and unreported. But the fact remains that others who have developed safer techniques, including the use of smaller

dosages, have reported large series of cases with no fatalities attributable to this method of anaesthesia. Resnick,[1] Thomas,[2] and Malkin[3] have reported between them more than 1,200 cases without a single anaesthetic death.

One of us has used spinal anaesthesia for caesarean sections over a period of more than ten years without observing the effects described by Mr. Stanley-Jones. Instead of the "massive vasodilatation of the largest and bloodiest organ in the body" we have invariably found caesarean sections under spinal anaesthesia to be associated with greatly reduced bleeding from the uterus, which contracts unusually well. Other authors have reported the same finding.[1 2 4] Recent work has shown that, provided adequate oxygenation and capillary circulation is maintained, even a severe fall in blood pressure need have no untoward effects on the patient. However, there is no difficulty in maintaining the blood pressure within normal limits with the aid of "methedrine."[5] The danger lies not so much in vasomotor "collapse" as in respiratory paralysis.[6 7] The gravid uterus, filling and distending the abdomen, interferes with the descent of the diaphragm. If to this is added intercostal paralysis extending to a high segmental level, grave anoxia may occur rapidly and insidiously. We have seen this happen on two occasions. Once in the presence of a large ovarian cyst, and once at the beginning of a caesarean section. In each case inhalation of 100% oxygen, or inflation of the lungs with oxygen, prevented any serious consequences, and in each case respiration returned to normal after removal of the abdominal tumour.

It is now becoming generally recognized that for caesarean section analgesia should be limited to the level of the xiphisternum. This means in practice a smaller dose than that usually used for appendicectomy, for instance. If this is done, respiratory embarrassment is avoided, but as a precaution an efficient means of inflating the lungs with oxygen should always be available for immediate use in emergency, and the uterus should be emptied while "controlled respiration" or 100% oxygen inhalation is maintained. The steep head-down tilt adopted in the belief that this will assist the blood pressure merely increases the respiratory embarrassment and makes matters worse. Also, when using "gravity-controlled" solutions it should be remembered that the spinal curves are altered in late pregnancy. We are now using an isobaric solution of amethocaine diluted with spinal fluid to a concentration of 1 in 1,000. We find that 8 to 10 ml. is quite adequate for caesarean section, although 12 ml. would normally be used for, say, a hysterectomy.

From the foetal standpoint spinal anaesthesia is ideal, as the babies usually cry as soon as their noses are born and they are free from the effects of respiratory depressants. The method is therefore especially valuable with premature or otherwise handicapped babies.

To deride as malpraxis a method which has over a period of years given such good results in the hands of experienced obstetricians is unworthy of your columns. We feel that so long as attention is paid to the precautions described spinal anaesthesia remains a safe and effective procedure in the absence of shock or severe bleeding, and it is especially valuable when caesarean section is performed in the interests of the baby.—We are, etc.,

DUNCAN BALLANTINE.
F. L. ROBERTSHAW.

Rotherham.

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Breast-feeding

SIR,—After having read Dr. James S. Hall (Jan. 8, p. 72), especially where he states that mothers are relinquishing the almost impossible task of synthesizing wholesome milk from snoek, scraps, and sausage meat, I feel still more ought to be added to the recent controversy on the subject of breast-feeding.

Although of course the present-day rations contain substantially more and better items than those mentioned by Dr. Hall, it is only too well known that most inadequate nourishment of the mother still assures a very high quality breast milk. I have spoken to doctors, and also with mothers, who have survived Hitler's concentration camps, and they were unanimous in saying that many children were born in these camps and all of them had to be breast-fed, as no other milk was available. The mothers often dying in the last stages of pulmonary tuberculosis still often managed to breast-feed their babies, and it was only in cases of extreme dehydration, when the mother was suffering from dysentery, etc., that one had the pathetic spectacle of seeing a mother putting the baby to a dry breast.

In addition I should like to say that Dr. Hall's belief of the equality of breast milk and the baby foods must be based on the knowledge that all the known chemical substances contained in breast milk are present in the artificial products. But even the most biochemically inclined paediatricians know that there are many other, mostly as yet unknown, factors present which make breast milk the superior nourishment.

The recognition of the importance of breast-feeding seems not only well established everywhere, but is increasing; this conclusion I draw from the fact that to-day in case histories, not only of babies but of younger and even older children, the mode of feeding as an infant has its definite place.—I am, etc.,

JOHN ABELS.

Whitehaven, Cumb.

SIR,—Picking up my *Journal* of Jan. 8 I find first (at p. 59) a very favourable review by Professor Charles McNeill of my book on breast-feeding, in which he remarks that "paediatricians proclaim and extol its importance"; and then, turning to a later page (p. 72), I find Dr. James S. Hall again taking up the cudgels for the bottle-fed infant. I am sure that Dr. Hall is right in saying that his cases of fully fed bottle babies compare very favourably with the under-fed breast babies which appear to be common in his practice. In my own practice, however, where *no* baby is underfed, whether it be on the breast or on the bottle, I do find a very real difference in morbidity rates between the two.

As feeding problems are attended to at the surgery, where I hold a weekly weighing and consultative session, my visits are genuinely for sickness. I have collected and recorded (the results are to be published shortly in the *Lancet*) the visits required during the first year of life by 100 consecutive babies in my practice. Briefly, the bottle babies required more than five times as many. Moreover, 73% of the breast-fed babies did not require a visit at all, as compared with 9½% among the artificially fed. In the present days of National Health Service and payment by capitation this argument for breast-feeding should at least appeal to the general practitioner, if only through his pocket.

I note that Dr. Hall, and the Dr. Hutchinson whom he quotes, are considering these children from the point of view of "adolescence or later life." I do not deny that the bottle-fed child may achieve both health and immunity in later life; but I prefer to save the mother the worry of the higher incidence of disease in infancy. What simply appals me is his picture of "maternal unhappiness and misery" caused by breast-feeding. None of my lactating mothers is unhappy or miserable. If they were, of course, they would undoubtedly underfeed their babies.—I am, etc.,

F. CHARLOTTE NAISH.

York.

SIR,—Dr. J. S. Hall (Jan. 8, p. 72) is still not impressed. In his first letter (Nov. 20, 1948, p. 919) he said: "I cannot determine that artificial feeding has any deterrent effect whatsoever. . . . I am of course open to conviction should sufficient modern evidence be available to the contrary." I have supplied him with some evidence; but he passes it off with a light laugh because it comes from America, and is, he infers, a sort of medical Marshall aid.

The reason I quoted American figures was that this is the largest series available. By a *petitio principii* Dr. Hall chooses to ignore the data on pyloric stenosis (despite the fact that the series was not lease-lent, but came from Westminster). Of 46 bottle-fed babies with pyloric stenosis 5 died. Of 100 breast-fed babies with the same disease none died. If Dr. Hall (or any other reasonable person) were told that his next infant was destined to suffer from congenital pyloric stenosis would he still allow it to be artificially fed?

It may be that in England now (owing to the lack of domestic help, or the snoek, or some other factor) artificial feeding is easier than breast-feeding; but, Sir, the *British Medical Journal* goes all over the world. Please do not let us disseminate any authority from the medical profession for a further decline in breast-feeding.—I am, etc.,

Bristol. HUGH R. E. WALLIS.

*** This correspondence is now closed.—ED., *B.M.J.*

Rhesus-testing in Pregnancy

SIR,—Doctors engaged in the practice of midwifery are now well aware of the importance of blood replacement in the treatment of the haemorrhages of pregnancy. Increasing use is therefore being made of the emergency resuscitation services which most maternity hospitals maintain for the purpose of transfusing women too ill to be removed into hospital.

It is, however, evident that some practitioners do not realize that blood transfusion cannot be undertaken with safety unless the rhesus status of the patient is known. The blood group can be determined at the bed-side, but the rhesus grouping can be ascertained only by a somewhat elaborate laboratory technique.

As one who has had some experience in emergency transfusions I write this letter to urge on all doctors responsible for the care of pregnant women the necessity to take steps to determine early in pregnancy the rhesus grouping of the patient. Too often one is summoned to women critically ill from blood loss only to find that the rhesus status is unknown, thus increasing the hazards of blood replacement. It is the bounden duty of all doctors who make themselves responsible for the care of the pregnant woman to see that the rhesus grouping is carried out as early as possible in the pre-natal period. The doctor who neglects this precaution is most certainly failing in his duty to the mother and her child.—I am, etc.,

Sheffield. W. J. CLANCY.

Senile Deterioration of the C.N.S.

SIR,—I was very interested to read the article by Dr. Trevor H. Howell on senile deterioration of the central nervous system (Jan. 8, p. 56). I must, however, disagree with the conclusions reached. In assessing central-nervous-system physical signs in this age group, one important factor seems to have been omitted—namely the state of the vascular system. In addition the defective absorption of vitamins must be considered—achlorhydria being a not uncommon "normal" finding in this age group.

Any attempt to explain these phenomena by a central lesion seems to me erroneous. I would say that the factors operating are: (1) peripheral vascular occlusion which, although not gross clinically, has been sufficient to impair the blood flow to the vasa nervorum of peripheral nerves; and (2) vitamin B deficiency, which has again led to peripheral nerve lesions and also to mid-brain lesions with pupillary changes.

It is then on a basis of a peripheral neuropathy that I would explain the lesions found. In support of this I note that the pyramidal tracts are normal in practically all cases, and lesions in the legs are more pronounced than in the arms—a not uncommon finding in peripheral vascular disease.—I am, etc.,

Leeds. RAYMOND C. GLEDHILL.

Cotton-dust Disease

SIR,—The following quotation is from your leading article (Dec. 18, p. 1069): "It seems more likely, however, that there are only two diseases, perhaps only one: mill fever is almost certainly the early stage of byssinosis, and the remaining two conditions are very similar to other diseases caused by mouldy organic matter such as grain, flax, hemp, jute, and bagasse." This is not correct. There are three distinct conditions, distinct clinically and occupationally.

1. *Mill Fever.*—This will affect anyone unaccustomed to cotton mills, whether spinning mills or weaving sheds. It is a very mild febrile attack with anorexia after a day in the mills. After a night's sleep it is gone, giving protection, which, however, disappears if the visits to the mills are discontinued. I have often experienced it.

2. *Strippers' and Grinders' Asthma.*—This is a very chronic disease which takes many years to develop. It only concerns men in spinning mills exposed to dust arising from raw-cotton bales. It is not seen in weaving sheds or among those who tend the spinning frames and self-acting mules to which the cotton sliver proceeds from the carding engines. I was the first to describe the condition in 1908.

3. *Weavers' Cough.*—This condition is only seen among cotton weavers, and only among weavers preparing cotton cloth for the bleachers and dyers. If the cotton thread being woven for this purpose gets damp on the warp beams, under conditions described by me in 1914, offensive moulds may grown on the threads, which become dark and smell badly. When such threads are woven the operatives experience epidemics of acute illness lasting several months and clinically resembling active pulmonary tuberculosis.

What byssinosis is I have often wondered. Βύσσος is a Greek word for linen.—I am, etc.,

Lossiemouth, Morayshire. EDGAR L. COLLIS.

Mallet Finger

SIR,—Perhaps it is wise first to define the deformity "mallet" finger as a lesion of the mechanism controlling extension of the terminal joint of any finger (the thumb is excluded).

From experience in the treatment of this very common industrial and domestic lesion we suspected that it was not a simple problem, and that the pathological anatomy of the tears might be as varied as the end results we observed to follow routine plaster immobilization with flexion of the proximal joint and hyperextension of the distal interphalangeal joint. Following this routine we were not unduly worried when flexion of the terminal joint persisted at the end of treatment; as Dr. W. J. Lloyd (Jan. 1, p. 30) has observed, most workmen can accommodate themselves to this deformity and are not concerned with the appearance of a useful working finger. (Precision workers, however, find the loss of complete control of the terminal joint of the index or middle finger a real working disability.) We were worried, however, by a group who after treatment complained of such pain in the distal interphalangeal joint that they could not return to work, and this pain persisted for a long period.

Therefore six years ago this hospital undertook a planned investigation of the problem, continued its close study for almost two years, allowed a period of time to elapse before assessing all the patients included in the study, and finally published[1] a detailed description of the varying surgical anatomy of these tears and a detailed account of the end results to be expected after surgical treatment.

From this study it is obvious, I think, that mallet finger cannot always be treated by a reassuring word, as Dr. Lloyd would seem to suggest. The open mallet finger caused by a grinding wheel, cutting or crushing violence—a not infrequent industrial injury—is an undisputed surgical matter.

The closed mallet finger, which may cause very troublesome and prolonged pain in the joint, is caused by the avulsion of a fragment of bone from the base of the terminal phalanx, taking with it a variable amount of articular cartilage. If the very disabling and painful traumatic arthritis of the joint is to be avoided, then early and accurate reduction of the fracture, in our view, is essential. If closed reduction fails, as it sometimes does, then early open reduction with internal fixation is essential.

The fracture type of mallet finger accounted for 25% of our series. Three-quarters of our patients had tears of the extensor tendon at varying levels, the level of the tear presenting its own problem in treatment—e.g., if any part of the tear was situated proximal to the joint, the prevention of adhesions between the tendon and the neck of the middle phalanx with the subsequent inability of the tendon to pull the joint into full extension still remains a problem.

The prognosis after surgical treatment of mallet finger seen early is not as bad as Dr. Lloyd's impressions indicate. In a close study of 61 consecutive mallet fingers treated by surgery, 20 regained full extension and a good range of flexion, the remainder had flexion deformities ranging from 10° to 30° and a good range of powerful controlled flexion. In the treatment of this condition there is undoubtedly an economic angle—we can both over-treat and under-treat: to do either may be unnecessarily expensive.

In my experience a common type of mallet finger is the partial tear in the middle-aged. The patient presents a terminal

joint with 20° to 30° flexion deformity with an ability to fully flex the joint and extend it to 20° or 30° of its full range. If such a tear is not associated with a fracture there is, I believe, a real place for the "reassuring word" in treatment. Most workmen can continue most jobs with such a finger, and within four or five weeks have accommodated themselves completely to the disability. The reassuring word, however, has no place in the economic treatment of the fracture type of mallet finger with extensive articular cartilage involvement. Symptoms of traumatic arthritis can be very prolonged. The treatment of painful arthritis by arthrodesis of the joint involves many months before the joint is so soundly fused that the finger has regained powerful and painless function.

The surgical and economic treatment of mallet finger is not a simple matter; it demands a clear understanding of the underlying pathology, very skilled technique in active treatment, and a degree of judgment in assessing those to treat and those to leave alone.—I am, etc.,

Birmingham Accident Hospital. WILLIAM GISSANE.

REFERENCE

1 *Brit. J. Surg.*, 1948, **35**, 397.

Classical Caesarean Section

SIR,—The recent correspondence on the merits and demerits of the classical caesarean operation has had a good deal of interest, mainly reminiscent, and the views of my own generation will of course stay coloured by the excitement we experienced some twenty years ago when we found that with the lower-segment operation post-caesarean peritonitis need no longer be a dread, and that at last we had a conservative alternative to the high forceps operations and the perforations. This then seemed more important even than the risks of later rupture of the scar. Nowadays, although the risks of infection no longer bear the same weight, most would agree that technically the lower-segment operation is much sounder, and until the other week I would have said from the experience of quite a number of cases that it could always replace the classical operation. I then met the following case.

A primigravida had a transverse lie which could not be corrected. The usual lower-segment operation was begun. The anaesthesia used was gas, ether, and curare. After opening the abdomen I could not correct the oblique lie and extract the child, either as a breech or a vertex, so firmly was the uterus moulded round the child. The situation was exactly similar to a failed internal version for a shoulder presentation. In order to deliver the child it was necessary to make a free longitudinal incision upwards into the body of the uterus. This left an unpleasant T-shaped wound to be stitched.

Part of the difficulty may have been due to the oxytoxic effect of the curare, and it might have been avoided by a deep relaxing anaesthesia, but deep anaesthesia is no proper solution to this sort of problem, and should I meet another case in which the uterus is contracted down on a transverse lie I would give serious thought to the advisability of an elective classical operation.—I am, etc.,

Liverpool. PERCY MALPAS.

Carcinoma of Cervix

SIR,—My attention has just been called by a doctor long in practice in Kenya to the letter of Dr. E. Malcolm Clark (Dec. 4, 1948, p. 999) in which he attributes the relative freedom of Jewish women from carcinoma of the cervix to "some racial factor which we do not as yet fully understand," and disputes my conclusion that they are protected from the disease by the circumcision of Jewish males in infancy. He records a personal experience of twelve cases of carcinoma of the cervix among 82 cancers in Kikuyu women.

My correspondent says, "I feel that in fairness to you Dr. Clark should have made it plain that circumcision as practised by the Kikuyu differs in some important respects from circumcision as practised by Jews. Kikuyu males are circumcised in or about puberty, and the operation is so performed that a large spur of preputial tissue remains, extending outwards on each side of the fraenum. It is very characteristic of the Kikuyu . . . the Kikuyu attach great importance to this tag of tissue."

It is hardly surprising that late and partial circumcision fails to give the female as much protection against cervical carcinoma as the complete operation in infancy. East Africa, with its complex mixture of circumcised and uncircumcised tribes and its primitive codes of sexual conduct, is not a field where unequivocal evidence on the subject can be obtained. In Fiji, on the other hand, where 90,000 circumcised Fijians live alongside 70,000 uncircumcised Indians without mixing, during the years 1925–32 the Suva Hospital admitted only three cases of cervical carcinoma in Fijian women and 26 in Indian women. I have no statistics of penile carcinoma in Fiji, but my attention was drawn specifically during my visit to its occurrence in Indians and its absence in Fijians.

The evidence from Fiji shows that circumcision, even done as late as puberty, has much protective value for the female. It also negatives the postulated racial immunity of Jewish women. Hoffman's statistics for Amsterdam (1919–29) showed a higher incidence of cancer of the breast, rectum, liver, and gall-bladder among Jews than among non-Jews.

In conclusion let me say that I have never advocated the general adoption of circumcision in this country. I believe that all its advantages could be obtained without removal of tissue by the simple operation of universal dorsal preputiotomy in the first days of life.

I am indebted to the medical superintendent of the Suva Hospital for the information that from January, 1947, to November, 1948, twelve cases of malignant uterine tumour in Indians have been admitted and only a single case in a Fijian.—I am, etc.,

London, W.1. W. SAMPSON HANDLEY.

Pre-suppurative Amoebic Hepatitis

SIR,—Dr. J. T. Harold (Dec. 11, 1948, p. 1034) states that no recent record exists of an amoebic abscess in a patient who had never been abroad. Dr. Francis Lowe (Jan. 1, p. 31) records a case, and I should like to report a second.

A male patient, aged 54 years, recently died in this hospital. He was admitted six months previously with an empyema of the right pleural cavity; there was no previous history of diarrhoea. Three months after admission he developed a typical amoebic dysentery, motile vegetative amoebae being found in the stools and later in the pleural pus. Surgical treatment and emetine therapy were of no avail, and the patient died six months after admission. A necropsy revealed an amoebic abscess of the right lobe of the liver which had tracked through the subphrenic space into the pleural cavity. The patient had lived nearly all his life in Bolton and had never left this country.

—I am, etc.,

Towneys Hospital, Bolton. M. W. JOHNSTONE.

Estimation of Prothrombin

SIR,—The report of the meeting of the Medical Society of London (Jan. 1, p. 26) contained statements concerning the control of dicoumarol therapy which might lead to misunderstanding. It is of great importance that ambiguities concerning the estimation of prothrombin should be avoided. Accidents have occurred in the past during dicoumarol treatment because of lack of appreciation of the many pitfalls encountered in the calculation of results and the confusion which exists in their interpretation.

Dr. Paul Wood is quoted as saying that the prothrombin concentration should be kept to "round about 30 to 40 mg. per 100 ml." Mr. Dickson Wright is said to have stated that "when less than 20 mg. per 100 ml. no dicoumarol was given. If the figure fell below 10 *units* (my italics) menadion bisulphite 30 mg. was given intravenously." In these two statements the prothrombin concentration is expressed both in "mg. per 100 ml." and in "units," neither of which is a customary procedure in this country. So far as I am aware there is no routine method for the estimation of prothrombin in milligrammes. It is nearly always expressed as a percentage of the concentration found in normal plasma, and it seems likely that the above quotations should read "30 to 40%," "20%," and "10%" respectively. If this is so, the minimum safe level advised by Mr. Dickson Wright is only half of that advocated by Dr. Wood.

It is not sufficiently realized that when prothrombin is estimated in dicoumarol plasma by a one-stage method[1,2] the result depends upon the technique employed. It varies with the thromboplastin[3] and also with the diluent used in the construction of the reference curve. Thus, if reference curves are

constructed by saline dilution of normal plasma and prothrombin is estimated in a dicoumarol plasma using venom-lecithin as thromboplastin,[2] the result will be higher than when brain emulsion[1] is used and very much higher than the result obtained with ox-lung extract.[4] If the prothrombin is estimated by the two-stage method[5] the result will probably differ from all three of those obtained by the one-stage procedures, though it will be nearest to that found by using venom-lecithin as thromboplastin.[4] Not only is the reference curve obtained when prothrombin-free plasma is used for diluting normal plasma entirely different from that obtained when saline is used, but curves obtained with different prothrombin-free plasmas differ from one another, depending on the method used for the removal of the prothrombin.[3]

It is therefore important that any criteria for the limits of safety in dicoumarol therapy should be accompanied by a precise definition of the method used for the estimation of prothrombin. Differences in technique probably account for the apparent discrepancy which appears in your report between the recommendations of Dr. Wood and Mr. Dickson Wright.—I am, etc.,

Reading. C. A. MAWSON.

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2 Hobson, F. C. G., and Witts, L. J., *J. Path. Bact.*, 1941, **52**, 367.
3 Conley, C. L., and Morse, W. I., *Amer. J. med. Sci.*, 1948, **215**, 158.
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Temperature Recording

SIR,—Professor Alan Moncrieff and Dr. B. J. Hussey (Dec. 4, 1948, p. 972), as well as the author of the annotation (p. 991) on temperature recording, overlooked the basic fact, often noted in "Any Questions?", "Correspondence", and "Notes and Comments" (*British Medical Journal* since 1943), that it takes ten minutes for the mercury clinical thermometer to reach stability with the temperature of the surrounding media irrespective of the site. Orally there may be an appreciable difference of 0.2°–0.5° F. (0.1°–0.25° C.) between a 2–3-minutes reading and one of 10 minutes; the same difference may also be noted between a site under the tip of the tongue (the usual site the nurse chooses) and further back at the side of the fraenulum.

While it requires great care—traumatic recto-urinary fistula from a thermometer may occur (*Medical Annual*, 1946, p. 53)—the rectal method, being the least sensitive to the atmospheric environment, is the best. In the ambulant patient the oral may be as misleading as the axillary; this was noted by the late Sir Thomas Lewis in the low-grade fever of bacterial endocarditis (*Diseases of the Heart*). Even during the diurnal cycle the maximum difference between oral and rectal (5–6 cm.) temperatures varies from 0.6°–1.2° F. (0.3°–0.7° C.), approximating on the upgrade and diverging on the downgrade, but the nexus may be neither proportionate nor constant. Allowance, of course, must be noted for the slight deviation of individual thermometers.

With low-grade fevers, as for example in rheumatic carditis, cited by the authors, the pyrexia may recur regularly or irregularly at times other than the usual maximum periods of 1 p.m., 7 p.m., or 11 p.m. Accurate thermometry would abolish much of the unnecessary routine laboratory tests in many chronic febrile diseases. Active rheumatic infection rarely may be present, as shown by the B.S.R. and leucocyte count, even if the normal rectal range of 97.7°–99.5° F. (36.5°–37.5° C.) is not exceeded; when the maximum rectal temperature is around 99° F. (37.2° C.) quiescence is assured (by the laboratory tests, the sleeping pulse, and the absence, at rest, of mild sensible perspiration day or night) in such cases.—I am, etc.,

Dublin. A. D. MACDWYER.

Spontaneous Amputation of Cervix

SIR,—As an interesting contrast with Mr. Walter Calvert's report (Jan. 8, p. 58) of difficult labour following surgical amputation of the cervix uteri, I beg to recall, in retirement, the following case.

Between 30 and 20 years ago a midwife summoned me to see something she did not understand in the vulva of a young primipara after a normal, easy labour. Delivery was complete; the placenta and membranes were normal, and there had been no undue haemorrhage.

I found it to be a plum-coloured fleshy mass which I had no difficulty in recognizing as the whole undilated cervix, 1–1½ in. (2.5–3.75 cm.) in length, the os being about ¼ in. (0.6 cm.) in diameter. Since it was attached by only a shred of tissue anteriorly I snipped it off and gave it subsequently to Professor Carlton Oldfield for the museum of the Leeds School of Medicine. It was clear that the child had been born through the split in the cervix at or near the internal os. The puerperium was normal.

Within two years the midwife called and told me that the patient had had another baby, born in a labour so quickly and easily that even she had not been able to get there in time. Again recovery was normal.

Can it be that a woman can amputate her own cervix better than even the most skilful gynaecologist?—I am, etc.,

Totland Bay, I.o.W. W. ARNOTT.

Lithium Ionization for Gout

SIR,—As one who has derived much personal benefit from lithium ionization in the treatment of an acute attack of gout, I deprecate the slighting reference to this treatment in the annotation on physiotherapy (Dec. 25, 1948, p. 1114). In the early days of my career I practised electrotherapy at a time when accurate medical ionization had only recently been introduced by Leduc and Lewis Jones, and I did some research and published papers on this subject.[1 2] The effect of lithium ionization in many cases of acute gout is extremely striking, because it commences immediately. I have had a patient come into my consulting-room on crutches who at the end of the treatment was already able to walk on the affected foot. Other patients have come to me repeatedly to abort successive attacks. I looked up the reference to Sir Henry Cohen's article, and this by no means makes the sweeping condemnation suggested in your annotation. Actually lithium ionization is not mentioned, and the reference to lithium is probably to oral medication.—I am, etc.,

London, W.1. N. S. FINZI.

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2 *British Medical Journal*, 1912, **2**, 1180.

POINTS FROM LETTERS

Manganese Therapy

Dr. C. A. ALLAN (Dundee) writes: Recent additions to the knowledge of the biochemistry of manganese have shown it to be concerned with antibody formation (Walbrum, L. E., *Acta path. microbiol. scand.*, 1944, **21**, 3; Petherick, M. H., *et al.*, *Proc. exp. Biol., N.Y.*, 1944, **59**, 254), and also that it is an activator of a number of important enzymes. . . . This has suggested to me that there may be other and as yet unexplored uses for manganese therapy, among which sensitization dermatitis, as a derangement of the body's normal defence mechanism, may possibly be included. With the object of testing this hypothesis manganese was recently used in two cases. The first was a bus driver, aged 39. From 1940–5 he was a motor transport driver in the Army, always in contact with diesel oil. He developed local skin irritation on legs and arms. From 1945–8 he had frequent absences from work as a bus driver; he was still in contact with diesel oil. He remained resistant to all treatment until colloidal manganese was used. Three doses of 1 ml. intramuscularly arrested the skin irritation, and he has remained free from any sort of this trouble to date, although still working daily with diesel oil. The second patient was a cook, aged 45. She was said to have had soap dermatitis for the past six months; arms and wrists affected, also neck. Prescription of soap, etc., had little effect. Again three doses of manganese, 1 ml., intramuscularly completely arrested this form of skin irritation. A routine examination of all the systems was made in each case and, seen recently, both have remained well.

Screening Aid for Mass Radiography

Dr. R. TREHARNE JAMES (Reading) writes: I was interested to read the description of a daylight screening aid for mass radiography units by Dr. S. W. Vivian Davies (Dec. 25, 1948, p. 1117). We have encountered the same difficulties as his unit in darkening our working sites and have for some months been using a similar screening hood. Though it is extremely useful it has one drawback, I think, in that the radiographer and his assistants are excluded from viewing the appearances. Time does not permit the examination to be repeated by several persons, nor does radiation dosage. Also it is desirable that the hood be removable easily and rapidly for laundering.

Obituary

STANLEY RAW, M.D., F.R.C.S.Ed.

Stanley Raw, who died with tragic suddenness at the age of 70 on Dec. 26, 1948, was one of the outstanding surgeons in the North of England. He was a student at the University of Durham, and he graduated M.B., B.S. in 1901. He proceeded M.D. in 1903, and took the F.R.C.S.Ed. in 1905. Raw was senior resident medical officer at the Sunderland Infirmary before starting in general practice in that town. He was later elected surgeon to the Children's Hospital. In 1915 he joined the R.A.M.C. and was surgeon to the Liverpool Merchants' Hospital, and spent some years in France. On his return he was appointed surgeon to the Royal Infirmary, Sunderland, and he gave up general practice. He also became surgeon to the Sunderland General Hospital. In 1931 the Durham colliery owners asked Mr. Raw to become medical officer to some of their groups. In 1945 he reached the retiring age and became consulting surgeon to the Royal Infirmary and to the General Hospital, but continued with his other work. He was chairman of the Sunderland Division of the B.M.A. in 1924–6 and a former president of the Northern Counties Clinical Society.

Raw was an accomplished surgeon with a leaning towards gynaecology. His results were good, and his surgical opinion was eagerly and widely sought. No one had more thought for the welfare of his patients, and his daily morning and evening rounds continued to the end. As a colliery medical officer, although there may have been disagreements from time to time, no pitman ever doubted his fairness, though sometimes his task was difficult. Raw's great interest was in the Royal Infirmary, Sunderland, and at endless discussions and innumerable committee meetings he did everything he could to advance its scope and improve its facilities. His ideas of hospital administration were much ahead of his time, and the Royal Infirmary, with which he was associated for forty-seven years, owes him an enormous debt. From 1930 to 1943 he was chairman of the medical board of the Infirmary. Sometimes a difference of opinion might become a personal disagreement and lead to temporary estrangement, but Raw himself had had some disappointments in earlier professional life.

He had climbed mountains, sailed small boats, and was golfing to the last. He was always advocating travel. Personally he was acute, astute, a wise counsellor, and a good companion. Being without children, he was most attached to his nephews and took great pride in their achievements. To those he was interested in or liked he was generosity itself. In his own world he was a very considerable figure; with some change of fortune he might have been much more widely known. Stanley was a personality with an English character; latterly he was an institution with a touch of magnificence. To his widow, who was his companion and helpmate for so many years, the sympathy of all his colleagues will be extended.—P. A.

Dr. H. L. Duke writes: As an Englishman who was privileged to enjoy close personal association with van Hoof during the eighteen months' sojourn in Uganda of the League of Nations Sleeping Sickness Commission, I should like to add a brief tribute to your account (Jan. 1, p. 34) of the personality of a very charming colleague. Van Hoof was a first-rate mixer, at home with all and sundry, high or low, black or white, peaceful or obstreperous. As a host he was ideal; an admirable raconteur, genial, with an acute sense of humour and a temperament imperturbable and placid. He loved a joke, practical or otherwise. He had a wonderful way with the natives, and his staff worshipped him and rendered him unquestioning loyalty. He knew all about a motor-car, and was a truly invaluable companion on the long empty stretches of the tsetse country in which the Commission spent so much time. His English was excellent, and his knowledge of human nature apparently inexhaustible. Yet one felt in those days that his main concern was his scientific work, and he was always ready at a moment's notice to switch off into a serious discussion of the programme. A gallant gentleman and a sad loss to his many friends.

Dr. JAMES RUST died at Malvern on Dec. 10, 1948, at the age of 79. After completing his early education at the Aberdeen Grammar School, he took his M.A. degree as a student of Aberdeen University in 1889, graduating M.B., C.M. in 1892, and proceeding M.D. in 1895. He was house-surgeon to the late Sir Alexander Ogston before taking up an appointment in China. Returning to England, he bought a practice in Gt. Colmore Street, Birmingham, where he remained until his retirement about ten years ago. Before his retirement he had been operated on for pyloric stenosis; he recovered from this operation and enjoyed fairly good health until last year, when signs of heart failure preceded his death from coronary thrombosis. Dr. Rust was a kind and generous friend, well loved by everyone, and he will be greatly missed. He was medical officer to the V.A.D. Auxiliary Hospital in Birmingham from May, 1915, to December, 1916, and was also divisional surgeon of the St. John Ambulance Brigade. He was a member of the panel committee for several years, and also prime mover in the formation of the Aberdeen University Club for Birmingham and the Midlands, of which he became the first president. He presented a silver cup to be competed for by the golfing members of the club. Dr. Rust, who was unmarried, never really recovered from the death of his sister, who was devoted to him. —A. H. M.

Dr. ALEXANDER BROWN JAMIESON, who since 1919 had been a member of the tuberculosis service of the Lancashire County Council, died suddenly at his home in Great Eccleston, Lancs, on Dec. 16, 1948. Dr. Jamieson graduated M.B., Ch.B. at Edinburgh University in 1910. For many years he worked in the districts served by dispensaries at Eccles, Leigh, Stretford, Farnworth, and Pendlebury, and also at the Peel Hall Pulmonary Hospital, Little Hulton. In February, 1945, he was appointed a member of the senior staff and became medical superintendent of the Elswick Sanatorium, near Kirkham, and consultant tuberculosis officer for the Fylde dispensary area. Recently the Manchester Regional Hospital Board established an enlarged dispensary area, bringing in Blackpool County Borough, and Dr. Jamieson became the chest physician of the Victoria Hospital in that town. Dr. Jamieson leaves a widow and one son. He was of a quiet disposition and was universally liked by his colleagues of the medical, nursing, and clerical staffs.

Medico-Legal

DURATION OF AGGRAVATION

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

A soldier contracted bronchitis while serving in the Army before the war. He was passed fit for service in 1939 and was put on guard duties which exposed him to the weather. In January, 1940, he became ill with influenza and a specialist reported that he was suffering from chronic bronchitis. For the next two years he was constantly on the sick list, and he was discharged in May, 1942. Seven months later a medical board found that his working capacity was reduced owing to shortness of breath. In 1944 his claim for a pension was rejected by a pensions appeal tribunal. In 1947 it was again rejected by a special tribunal which found that he had been in the Army for nearly three years, during which he was subject to no conditions which could be supposed to have exercised any influence on his bronchitis. He appealed to the court, and Mr. Justice Denning[1] held that the finding of the tribunals could not be reconciled with the evidence, and that the only reasonable conclusion was that at the date of the appellant's discharge his complaint had been aggravated by war service.

The question was raised whether the aggravation due to war service had not passed away, and whether a tribunal making such an award could say for how long the aggravation had continued, and if and when it had passed away. His lordship thought a tribunal could do so, provided that both parties had notice that the point was to be considered. A claim made immediately on discharge, he said, took some time to reach a pensions appeal tribunal, and the claimant usually pleaded not only that the disease was aggravated at the date of discharge but also that it remained aggravated at the date of the hearing. When the Minister rejected such a claim, he said that the

[1] *Ansell* v. *Minister of Pensions*, 1948, 2 All E.R. 789.

disease was not aggravated either at the date of discharge or at the date of the hearing. The evidence before the tribunal included medical evidence which brought the position right down to the date of the hearing. It was therefore obviously undesirable that the tribunal should confine itself to the moment of discharge and leave the question of duration to another tribunal. As a rule it was right and proper that the tribunal should consider not only the question whether aggravation remained at the date of discharge but also the question whether it remained aggravated at the date of the hearing, and, if it had passed away, at what date it did so. So long as both parties had notice of the case they would have to meet, it was open to the tribunal to find that any aggravation passed away at any time since discharge. The judge then remitted this case to a tribunal to decide whether the aggravation still remained, or at what date it had passed away.

Universities and Colleges

UNIVERSITY OF ST. ANDREWS

The following candidates have been approved at the examination indicated:

FINAL M.B., CH.B.—H. M. G. Ewan, Jean A. Houston, Maria I. Insh, B. R. B. Lumb, A. H. Moyes, Phyllis Norrie, W. P. R. Rintoul, A. J. Smith.

UNIVERSITY OF LONDON

A course of two Special University Lectures on "The Use of Radioactive Tracers in Biological Research" will be given by Professor F. A. Paneth, F.R.S., at the School of Pharmacy, 17, Bloomsbury Square, London, W.C., on Wednesday and Thursday, Jan. 26 and 27, at 5.30 p.m.

A Special University Lecture on "Virus Research and the Virus Problem" will be given by Dr. Pierre Lépine, of the Institut Pasteur, Paris, at the London School of Hygiene and Tropical Medicine, Keppel Street, W.C., on Tuesday, Feb. 8, at 5.15 p.m.

At the Foundation Day ceremony on Nov. 18, 1948, the honorary degree of D.Sc. was conferred on Sir Alexander Fleming, M.B., F.R.C.P., F.R.C.S., F.R.S.

Dr. E. R. Boland, Dean of the Faculty of Medicine, has been appointed a member of the Academic Council for 1948–9.

Professor J. M. Mackintosh has been appointed delegate of the University at the Health Congress of the Royal Sanitary Institute to be held at Brighton from May 23 to 27, and Professor Wilson Smith delegate at the fifth International Congress of Comparative Pathology to be held at Istanbul in May.

The following have been recognized as teachers of the University in the subjects indicated in parentheses: *St. Bartholomew's Hospital Medical College:* Mr. J. C. Hogg and Mr. N. A. Jory (Oto-rhino-laryngology); Mr. John Howkins (Obstetrics and Gynaecology); Sir Archibald McIndoe, Mr. D. F. E Nash, Mr. O. S. Tubbs, and Mr. E. G. Tuckwell (Surgery); Dr. B. Rait-Smith (Anaesthetics). *St. Thomas's Hospital Medical School:* Mr. T. W. Mimpriss (Surgery); Dr. J. S. Richardson (Medicine); Mr. N. H. Ll. Ridley (Ophthalmology). *Middlesex Hospital Medical School:* Dr. C. C. Chesterman (Tropical Medicine). *Charing Cross Hospital Medical School:* Dr. R. J. Clausen (Anaesthetics); Dr. R. J. Harrison (Anatomy); Mr. J. G. Milner (Ophthalmology); Mr. H. S. Sharp (Oto-rhino-laryngology); Dr. T. F. Tierney (Radiology, probationary for two years). *Westminster Medical School:* Dr. F. Dudley Hart (Medicine); Mr. B. St. J. Steadman, M.R.C.S., L.R.C.P., and Mr. R. S. Taylor, M.R.C.S., L.R.C.P. (Dental Surgery). *Royal Free Hospital School of Medicine:* Dr. J. D. S. Flew (Obstetrics and Gynaecology). *King's College Hospital Medical School:* Dr. J. D. N. Hill (Mental Diseases (Psychiatry)). *London School of Hygiene and Tropical Medicine:* Dr. I. E. McCracken (Public Health).

The following candidates have been approved at the examination indicated:

M.D.—*Branch I (Medicine):* P. Arnold, S. Balasingam, F. A. Binks, V. M. Borrelli, W. F. Cavenagh, F. B. Charatan, A. G. C. Cox, R. H. Cutforth, J. J. Y. Dawson, V. Edmunds, I. G. Fergusson, I. W. Gallant, O. Garrod, I. Gilbert, Audrey Hanson, J. C. Harland, G. P. Hartigan, W. M. R. Henderson, J. Henneman, J. W. Jordan, P. G. Keates, C. W. Kesson, H. A. Leggett, R. R. H. Lovell, K. M. Mackenzie, J. C. H. Maidment, T. P. Mann, R. M. Mayon-White, I. C. L. Patch, J. H. S. Pettit, T. R. E. Pilkington, A. Poteliakhoff, F. Riley, R. W. Rowan, J. R. Sinton, H. E. Thomas, H. R. Thomson, M. H. West, J. B. Wild. *Branch II (Pathology):* J. A. H. Brown, M. G. H. Cooray, R. H. Gorrill, N. F. C. Gowing, R. H. Heptinstall, J. Marks, R. D. de A. Seneviratne, D. A. Stanley, J. B. Walter, A. J. N. Warrack. *Branch III (Psychological Medicine):* T. G. Williams. *Branch IV (Midwifery and Diseases of Women):* Aileen M. Dickins. *Branch V (Hygiene):* J. B. M. Davies, R. E. Lane. *Branch VI (Tropical Medicine):* D. A. B. Hopkin.

UNIVERSITY OF LIVERPOOL

The following candidates have been approved at the examinations indicated:

M.D.—C. D. Alergant, H. Angelman, H. B. N. Jennings, J. Mills, R. H. M. Stewart, R. H. White-Jones, F. J. Zacharia

M.CH.ORTH.—G. W. Baker, R. F. Browne, N. A. G. Covell, R. H. Dawson, T. Denness, P. K. Duraiswami, M. J. Gallagher, J. R. Hughes, W. A. Hugh-Smith, A. F. McSweeny, A. B. D. Minnaar, L. Mirkin, B. Mukopadhaya, R. F. O'Driscoll, W. H. G. Patton, J. H. G. Robertson, A. K. Saha, G. L. Shatwell, C. C. Slack, E. A. Smyth, I. D. Sutherland, W. J. Virgin.

D.P.H.—*Part I:* Kaziniera H. Abramowicz, D. J. Cusiter, K. G. Koshi, H. McNicholl, D. A. W. Nugent, G. P. Reed, H. D. Sutherland, W. F. Wille.

CERTIFICATE IN PUBLIC HEALTH.—E. G. Donovan, H. B. Kilroe, Betty J. McConnell, Margaret M. Omeara, R. B. S. Smith, Corris Venables.

M.B., CH.B.—*Part III (Old Regulations):* C. E. Arkle, N. O. Ascroft, G. Bilsbarrow, J. D. E. Edwards, Elspeth M. Evans, J. A. Finnigan, Gwen E. Hughes, T. J. M. Hughes, Gwenyth H. Kendrick, J. H. Murray, N. C. W. Owen, W. H. Parry, Enid Rees, Joyce L. Rowley. *Passed in separate subjects:* S. Plumpton (Medicine, Obstetrics, and Gynaecology). *Part II (Old Regulations):* Rosemary J. Bolam, K. W. Brewster, W. Ellis, G. Jones, R. E. Jones, J. G. Kay, G. K. S. Roberts, A. Rootstein. *Part I (Old Regulations):* Marjorie J. Burke, J. J. Cameron, Judith E. Coope, B. L. Evans, A. K. Frazer, Lavinia Freeborough, A. W. G. Housby, Doreen Jacobs, D. H. Jones, Eileen P. McLeavey, Mary W. Malone, E. N. Marks, Jean A. Raffle, G. F. Stone. *Passed in separate subject:* Ludwicka Haas (Pharmacology and General Therapeutics).

[1] Distinction in Obstetrics and Gynaecology.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

FACULTY OF ANAESTHETISTS

The first annual general meeting of the Faculty of Anaesthetists will be held on March 16, at 3.30 p.m. Notice of motions for decision at the meeting must be received by the secretary not later than ten days before the meeting. At 5 p.m., the first Joseph Clover Memorial Lecture will be given by Mr. A. D. Marston. On the same day, the first anniversary dinner of the Faculty will be held, and all Fellows and Members of the Faculty are eligible to attend. Owing to the limited accommodation available it will not be permissible for Fellows and Members to have more than one ticket. The dinner will be at 7.30 for 8 p.m., and the dress will be dinner jacket. Applications for tickets, accompanied by cheques for £2 2s., should be made as soon as possible to the secretary, Faculty of Anaesthetists, Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C.2.

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW

Professor J. R. Learmonth, C.B.E., F.R.C.S., will deliver the Dr. John Burns Lecture in the Hall of the Faculty (242, St. Vincent Street, Glasgow) on Wednesday, Jan. 26, at 5 p.m. The title of the lecture is "Some Aspects of the Surgery of the Spleen." All medical practitioners are invited to attend.

The Services

The President of the French Republic has conferred the decoration of Insignia of Chevalier of the Legion of Honour upon Captain B. J. Fowler, R.A.M.C., surgeon at the military hospital in Tobruk, in recognition of valuable services rendered by him on the occasion of a mine explosion in April, 1947.

The *London Gazette* has announced the following appointments and mentions in dispatches in recognition of gallant and distinguished services in Palestine. The periods are indicated in parentheses:

O.B.E. (Military Division).—Lieutenant-Colonel (Temporary) G. H. C. Ovens, R.A.M.C. (Sept. 27, 1947, to March 26, 1948).

M.B.E. (Military Division).—Major (Temporary) W. J. G. Brunt, R.A.M.C. (Sept. 27, 1945, to March 26, 1946).

Mentioned in Dispatches.—Majors (Temporary) J. A. G. Horton and A. Steer, R.A.M.C. (Sept. 27, 1945, to March 26, 1946); Colonel W. H. O'Riordan, R.A.M.C. (March 27, 1946, to Sept. 26, 1946); Colonel A. J. Beveridge, O.B.E., M.C.; Lieutenant-Colonel R. R. Leaning, Major A. D. Young, D.S.O., Majors (Temporary) J. T. Landau and S. A. Lane, Captains C. G. H. Bourhill, A. C. Cobban, and D. Peebles, R.A.M.C. (Sept. 27, 1946, to March 26, 1947); Major W. R. Lamb, M.C., Captains K. W. Leech, E. S. Machell, and H. R. Turner, Captain (Temporary) W. A. Reynolds, R.A.M.C. (March 27, 1947, to Sept. 26, 1947); Lieutenant-Colonel (Temporary) S. Ward, Majors (Temporary) A. S. Douglas, D. F. Freebody, and J. G. Hoult, Captains M. P. Durham, G. L. MacKay, C. G. Teverson, and R. A. L. Wenger, Captains (Temporary) I. A. MacGregor and W. A. Reynolds, R.A.M.C. (Sept. 27, 1947, to March 26, 1948); Lieutenant-Colonel (Temporary) J. C. Lambkin, Major (Temporary) (Miss) E. C. Brownlie, Captains A. Batty-Shaw, M. P. Durham, M. M. Herbert, and H. A. F. Mackay, Lieutenant W. Hayhurst, R.A.M.C. (March 27, 1948, to June 30, 1948).

No. 1

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended Jan. 1.

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for: (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.

Figures of Births and Deaths, and of Deaths recorded under each infectious disease, are for: (a) The 126 great towns in England and Wales (including London). (b) London (administrative county). (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.

A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

Disease	1949 (a)	(b)	(c)	(d)	(e)	1948 (Corresponding Week) (a)	(b)	(c)	(d)	(e)
Cerebrospinal fever	28	3	18	2	—	55	4	26	1	2
Deaths		2	—				2	1		
Diphtheria	142	18	26	5	2	225	22	31	10	3
Deaths	3	—	—	—	—	5	1	—	—	—
Dysentery	53	9	39	—	—	86	11	19	1	—
Deaths				—	—				—	—
Encephalitis lethargica, acute	—	—	—	—	—	2	—	1	—	—
Deaths		2					—			
Erysipelas			35	9	2			31	11	2
Deaths		—					1			
Infective enteritis or diarrhoea under 2 years				36					36	
Deaths	39	5	8	2	5	59	3	11	3	5
Measles*	11,121	294	41	81	53	4,490	251	163	174	23
Deaths†			—	1	—	1	—	1	—	—
Ophthalmia neonatorum	48	5	16	—	—	58	5	10	1	—
Deaths										
Paratyphoid fever	3	1	—	1 (B)	—	39	2	—	—	—
Deaths	—	—	—	—	—	—	—	—	—	—
Pneumonia, influenzal	1,050	59	6	6	4	1,098	99	3	5	10
Deaths (from influenza)‡	29	3	2	—	—	35	7	5	—	1
Pneumonia, primary			373	54				284	41	
Deaths	330	62		14	11		60		18	12
Polio-encephalitis, acute	3	—				4	—			
Deaths							—			
Poliomyelitis, acute	20	—	5	3	—	59	7	5	2	—
Deaths§	2	—					—			
Puerperal fever		—	9		—		3	6		1
Deaths										
Puerperal pyrexia‖	66	4	5	—	—	112	11	11	—	—
Deaths		—					—			
Relapsing fever	—	—			—	1	—			—
Deaths										
Scarlet fever	1,125	54	245	109	42	1,786	125	298	42	34
Deaths†			—	1	—	—	—	—	—	—
Smallpox	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Typhoid fever	7	1	—	2	—	5	—	2	1	1
Deaths	2	1	—	—	—	—	—	—	—	—
Typhus fever	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Whooping-cough*	2,015	133	50	70	15	1,891	135	20	65	9
Deaths	10	—	2	1	1	5	—	—	1	—
Deaths (0–1 year)	359	44	56	30	15	420	41	73	28	22
Infant mortality rate (per 1,000 live births)										
Deaths (excluding still-births)	6,362	1047	743	242	121	5,720	968	665	236	165
Annual death rate (per 1,000 persons living)			15·0	15·1				13·8	14·9	
Live births	7,253	1172	898	379	280	9,608	1535	963	470	291
Annual rate per 1,000 persons living			18·1	23·7				19·4	29·7	
Stillbirths	186	31	23			227	31	26		
Rate per 1,000 total births (including stillborn)			25					26		

* Measles and whooping cough are not notifiable in Scotland, and the returns are therefore an approximation only.

† Deaths from measles and scarlet fever for England and Wales, London (administrative county), will no longer be published.

‡ Includes primary form for England and Wales, London (administrative county), and Northern Ireland.

§ The number of deaths from poliomyelitis and polio-encephalitis for England and Wales, London (administrative county), are combined.

‖ Includes puerperal fever for England and Wales and Eire.

EPIDEMIOLOGICAL NOTES

Influenza

Deaths certified as due to influenza in the 126 great towns rose to 47 in the week ended Jan. 8, compared with 29 in the previous week. This is the largest weekly total since the spring of 1947. The rise is not disproportionate for the season and suggests that virus influenza had not reached epidemic proportions in England and Wales. There is, however, confirmation that influenza has spread across Europe from the south-east. The disease appeared in Italy early in December, 1948, and had crossed to the Haute-Savoie about Dec. 15. It spread up the eastern border of France between Dec. 15 and Dec. 20 and affected most of the country, sparing only a few departments. It seems that it was not present in Paris until about Dec. 20, and the attack rate increased about Christmas. In Paris it took about fourteen days for the disease to reach a maximum incidence. There is, so far, no sign of regression. A conservative estimate of incidence up to the present is 15% of the population of France. Some communities have experienced attack rates up to 30 or even 40%.

The spread to the Northern European countries continues. In Holland the disease entered at Eindhoven on Dec. 31 and appeared in Leiden seven days later. Outside France and Italy, according to telegraphic reports received in Geneva up to Jan. 11, there had been no abnormal increase in influenza in Scandinavia, Spain, Hungary, and the American zone of Germany. The disease was prevalent in the Vorarlberg Tyrol of Austria. In Switzerland thirteen cantons were affected, particularly Tessin, Geneva, and Basle. To the east there were small foci in certain towns in Turkey, but no epidemic. In Northern Europe the epidemic was still confined to South Holland.

Clinical Features.—The disease occurring in France is typical and easily distinguished from the benign seasonal catarrhs. The average case has an abrupt onset with headache, weakness, muscle pains, and fever. Apart from a sore throat, signs referable to the respiratory system are few at onset. In the ordinary case the illness lasts seven days and is followed by some debility. Complications are few and encephalitis has not been reported. Pulmonary complications have killed elderly people. A few deaths from acute pulmonary oedema in the first thirty-six hours of the illness, particularly in children under 2, have been mentioned.

Virus.—In a previous announcement "virus B" was mentioned. It now seems more probable that the virus mainly responsible is more closely related to virus A. Identification experiments at the World Influenza Centre laboratory at Hampstead are incomplete.

Local Health Authorities.—The Ministry of Health has advised local authorities in England and Wales that the increased incidence of influenza in parts of Europe may foreshadow an early outbreak in this country, although there are no signs of this at present. It is suggested that medical officers of health and local authorities should plan in advance the arrangements which may have to be made if there is an unusually heavy incidence of influenza. These measures will be related to the local health authorities' services under Part III of the National Health Service Act, and the home nursing and domestic help services may both have to meet considerable extra demands. In a circular issued recently the Ministry urges that at the moment local health authorities should do no more than shape precautionary plans against the possibility of a large-scale outbreak.

Annual Report of England and Wales for 1946

The crude death rate during 1946 was 12.0 per 1,000, but when corrected for age the Comparative Mortality Index was 0.881 and was the lowest value yet recorded. Infant mortality was 42.85 per 1,000 live births and was the lowest value ever recorded. The neonatal mortality of 24.46 was 0.30 below the value for 1945 and 0.11 above the value for 1944. Maternal mortality decreased from the previous lowest level of 1.47 in 1945 to 1.24 per 1,000 total births. The death rates per million children under the age of 15 were 40 for diphtheria, 3 for scarlet fever, and 22 for measles, and were the lowest rates ever recorded; the rate for whooping-cough was 91, an increase of 12 on the 1945 rate but appreciably lower than the pre-war average.

Discussion of Table

In *England and Wales* during the week under review there were increases in the notifications of measles 2,162, acute pneumonia 258, whooping-cough 224, diphtheria 42, and dysentery 23. The only decrease was in the incidence of scarlet fever 29.

The largest increases in the notifications of measles were Lancashire 484, London 184, Staffordshire 157, Cheshire 146, Somerset 117, and Berkshire 116. The largest changes in the incidence of whooping-cough were increases in Lancashire 96

and Warwickshire 52, and a decrease in Glamorganshire 50. There was an increase of 12 in the incidence of diphtheria in London. Little change was recorded in the local incidence of scarlet fever. A rise in the notifications of acute pneumonia occurred in every region of the country.

The largest returns of dysentery were Lancashire 12 (Liverpool C.B. 7) and London 9 (Hackney 7). Two of the 3 cases of paratyphoid fever and 4 of the 7 cases of typhoid fever were notified in Lancashire. Only two counties had more than one notification of acute poliomyelitis: Worcestershire 4 (Kidderminster M.B. 3) and Derbyshire 2, both notified in Whaley Bridge U.D.

In *Scotland* there were decreases in the notifications of whooping-cough 80 and measles 45, while rises were reported for acute primary pneumonia 36 and dysentery 11. A small increase in the incidence of dysentery was recorded in all except the northern areas. The rise in the incidence of pneumonia occurred mainly in the north-eastern and eastern area.

In *Eire* increases of 52 in the notifications of measles and of 31 in the notifications of pneumonia were the only changes of note. The largest outbreak of measles was at Laoighis, Athy No. 2 R.D. 32.

In *Northern Ireland* a fall from 11 to 2 in the notifications of diphtheria was the chief feature of the returns.

Quarterly Returns for Northern Ireland

The birth rate for the September quarter was 21.5 per 1,000 and was 1.3 below the average for the third quarters for the preceding five years. Infant mortality was 41 per 1,000 registered births and was 12 below the five years' average. The general death rate was 9.9 per 1,000 and was 0.4 below the average for the five third quarters. Deaths attributed to the principal infectious diseases numbered 56 and included 26 from infantile diarrhoea and enteritis, 14 from measles, and 10 from whooping-cough. No deaths were due to diphtheria. Deaths from pulmonary tuberculosis numbered 166 and from other forms of tuberculosis 48; these totals were 14 and 9 respectively below the averages of the five preceding quarters.

Week Ending January 8

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 1,022, whooping-cough 2,306, diphtheria 126, measles 13,185, acute pneumonia 1,181, cerebrospinal fever 43, acute poliomyelitis 19, dysentery 81, paratyphoid 2, and typhoid 4.

Medical News

Dr. Anne Gibson Survives Air-crash

On the basis of information in the daily press we announced last week the "death" on Jan. 5, 1949, as the result of an air crash, of Dr. Anne Gibson, of St. James's Hospital, Balham, S.W.12. Happily Dr. Gibson survived the disaster. We much regret the error and any distress the announcement may have caused Dr. Gibson, her relatives, and her friends. Dr. Gibson was a passenger in an airliner which crashed in Brazil while on its way to Chile. The medical superintendent of St. James's Hospital informs us that a message has recently been received from Dr. Anne Gibson stating that she is alive and well.

King Edward's Hospital Fund

His Majesty the King has sent an annual subscription of £1,000 for 1949 to King Edward's Hospital Fund for London. The Fund has also received a further instalment of £150,000 from the Nuffield Trust for the Special Areas. In founding this Trust Lord Nuffield provided that any sums that might be available by way of repayment of loans or otherwise from his Trust for the Special Areas should pass to King Edward's Hospital Fund for London. A total sum of £1,150,000 has now been received.

Prospective Parliamentary Candidate

Dr. A. D. D. Broughton has been chosen by Batley and Morley Labour Party (Yorks) as prospective candidate in the by-election caused by the death of Captain Beaumont. In 1945 Captain Beaumont had a majority for the Socialist Party of 11,592.

London County Medical Society

At the annual general meeting of the London County Medical Society on Jan. 5 the following officers were elected: president, Dr. C. D. Coyle; vice-president, Mr. Iain Matheson; hon. treasurer, Dr. L. T. Hilliard; hon secretary, Mr. J. Gabe. A full programme for the forthcoming year is being arranged. The next meeting of the Society will be held on Thursday, Feb. 3, at 4.30 p.m. at Mile End Hospital, Bancroft Road, E.1. Dr. A. F. Mohun and Dr. J. Rubie will open a discussion on streptomycin in the treatment of tuberculosis. The annual subscription of five shillings is now due and should be sent to Dr. L. T. Hilliard, the Fountain Hospital, S.W.17. Membership is open to any medical practitioner. Inquiries should be addressed to Mr. J. Gabe, F.R.C.S., St. Alfege's Hospital, Vanbrugh Hill, S.E.10.

French Award

The French Government has recently conferred the Médaille de la Reconnaissance Française on the following: Lord Moran, P.R.C.P., Dr. K. E. Eckenstein, Dr. N. M. Goodman, Dr. Dorothy Gough, Mr. Holmes Sellors, Dr. L. E. Houghton, Dr. J. Moore, Dr. A. J. Morland, Dr. Eugene Nassau, Dr. P. G. Stock, Dr. R. E. Stuart-Webb.

COMING EVENTS

National Health Service Act

Dr. Charles Hill, Secretary of the Association, will address a meeting of members of the Metropolitan Counties Branch on Thursday, Jan. 27, at 8 p.m., in the Great Hall, B.M.A. House, Tavistock Square, London, W.C. The title of the address will be, "Terms of Service."

Guild of St. Luke, SS. Cosmas and Damian

A dinner-dance organized by the Westminster Branch of the Guild of St. Luke, SS. Cosmas and Damian will be held at Dorchester Hotel, Park Lane, London, W., on Thursday, Feb. 3, at 7.30 p.m., when guests will be received by His Eminence Cardinal Griffin. Tickets (£1 11s. 6d. each) may be obtained from the honorary secretary, 5, Wimpole Street, London, W.1 (Tel.: Langham 3230).

Edinburgh Lectures

A series of Honyman Gillespie Lectures has been arranged, in association with the Edinburgh Postgraduate Courses, to take place during the spring term in the West Medical Theatre of Edinburgh Royal Infirmary on Thursdays, Feb. 10, 17, and 24, at 5 p.m. The lectures are open to all graduates and senior students. Details will be published in the diary columns of the *Journal* week by week.

Public Health and Hygiene

The Royal Institute of Public Health and Hygiene announces that the next course of instruction for the Certificate in Public Health and for the Diploma in Industrial Health (Part I) will commence on March 25. Prospectuses, enrolment forms, and full details may be obtained from the secretary of the Institute, 28, Portland Place, London, W.1.

Banting Memorial Lecture

Professor John Beattie, Bernhard Baron Research Professor at the Royal College of Surgeons of England, will deliver the Banting Memorial Lecture at Toronto next month.

Rheumatic Diseases Conference

The 7th International Congress on Rheumatic Diseases will be held in New York City on May 30–June 3 under the auspices of the International League against Rheumatism (*Journal*, Dec. 4, 1948, p. 1003). The date by which information on the presentation or discussion of papers is requested has been extended to Feb. 15. Information may be obtained from Dr. Ralph Pemberton, 1901, Walnut Street, Philadelphia, Pennsylvania, U.S.A.

Congress of Life Assurance Medicine

The Third International Congress of Life Assurance Medicine will be held in Rome on June 6–9. The titles of the subjects for discussion and the names of the opening speakers are as follows: "Medical Examination on Life Assurance—Its Difficulties and Pitfalls": Professor H. Courcoux (Paris), Dr. R. de Beden (Trieste). "The Influence of Heredity on Mortality": Professor R. Sand (Brussels), Professor V. Bisceglie (Catania). "Heart Disease and Life Assurance"—(*a*) "Valvular Defects": Dr. H. D. E. Milders (Rotterdam), Dr. Terence East (London); (*b*) "The Arrhythmias": Dr. J. R. B. Hutchinson (Washington), Dr. V. Mortensen (Copenhagen). "The Lessons of the War in Relation to Preventive Medicine": Professor Ch. Richet (Paris), Dr. F. Kaufman (Zurich), Professor G. Mazzetti (Florence), Dr. A. Starna (Rome). All doctors interested in life assurance medicine are entitled to attend, and any wishing to take part in the discussions should communicate with the secretary of the Congress at Piazza San Bernardo, 101, Rome, not later than the end of March, 1949, sending a summary of their communication, which should not exceed 200 lines and which should be accompanied if possible by translations in French, German, and Italian, the three official languages of the Congress. Information about travelling arrangements and accommodation can be obtained from the secretary of the Life Assurance Medical Society—Dr. Kenneth Dickson, 3, Lombard Street, E.C.3.

SOCIETIES AND LECTURES

Saturday

SOUTH EAST METROPOLITAN REGIONAL TUBERCULOSIS SOCIETY.—At Preston Hall, Aylesford, Kent, Jan. 22, 10.30 a.m. General meeting.

Monday

UNIVERSITY COLLEGE LONDON.—At Physiology Theatre, Gower Street, London, W.C., Jan. 24, 4.45 p.m. "*The Ultracentrifuge and Electrophoresis Apparatus in Protein Research*," by Dr. P. Johnson, Ph.D.

Tuesday

EUGENICS SOCIETY.—At Royal Society, Burlington House, Piccadilly London. W., Jan. 25, 5.30 p.m. "*The Work of the Galton Laboratory*," by Professor L. S. Penrose.

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, Leicester Square, London, W.C.—Jan. 25, 5 p.m. "*Histopathology of the Skin*," by Dr. I. Muende.

INSTITUTE OF UROLOGY.—At St. Paul's Hospital, Endell Street, London, W.C., Jan. 25, 11 a.m. "*Infections of Urogenital Tract Due to Candida Albicans*," by Dr. W. N. Mascall.

UNIVERSITY COLLEGE LONDON.—At Physiology Theatre, Gower Street, London, W.C., Jan. 25, 5.15 p.m. "*Respiration*," by Dr. E. A. Underwood.

Wednesday

BRITISH ASSOCIATION OF PHYSICAL MEDICINE.—At St. Thomas's Hospital, London, S.E., Jan. 26, 5.30 p.m. "*How to Examine a Joint*." Demonstration by Dr. J. H. Cyriax.

INSTITUTE OF PSYCHIATRY (UNIVERSITY OF LONDON).—At Maudsley Hospital, Denmark Hill, London, S.E., Jan. 26, 2.45 p.m. "*The Thalamus*," by Professor W. E. Le Gros Clark.

INSTITUTE OF UROLOGY.—At St. Paul's Hospital, Endell Street, London, W.C., Jan. 26, 11 a.m. "*Ocular Manifestations of Venereal Disease*," by Dr. A. H. Harkness.

LONDON UNIVERSITY.—At School of Pharmacy, 17, Bloomsbury Square, London, W.C., Jan. 26, 5.30 p.m. "*The Use of Radioactive Tracers in Biological Research*," by Professor F. A. Paneth, F.R.S.

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW, 242, St. Vincent Street, Glasgow.—Jan. 26, 5 p.m. "*Some Aspects of the Surgery of the Spleen*," by Professor J. R. Learmonth.

Thursday

DEWSBURY: STAINCLIFFE GENERAL HOSPITAL.—Jan. 27, 9 p.m. "*Clinical Problems in the Diagnosis and Treatment of Thyroid Disease*." by Professor R. E. Tunbridge.

INSTITUTE OF UROLOGY.—At St. Paul's Hospital, Endell Street, London, W.C., Jan. 27, 11 a.m. "*Chancroid*," by Dr. W. N. Mascall.

LONDON UNIVERSITY.—At School of Pharmacy, 17, Bloomsbury Square, London, W.C., Jan. 27, 5.30 p.m. "*The Use of Radioactive Tracers in Biological Research*," by Professor F. A. Paneth, F.R.S.

MEDICO-LEGAL SOCIETY.—At 26, Portland Place, London, W., Jan. 27, 8.15 p.m. "*The Coroner, the Doctor, and the Public*," by Robert Forbes.

ROYAL SANITARY INSTITUTE.—At Town Hall, Wolverhampton, Jan. 27, 10.15 a.m. Discussions: "*The Present Housing Problem—Is New Legislation Necessary?*" to be opened by Mr. F. B. Hartley. "*The Scope of Care Work and Who Should Undertake It*," to be opened by Dr. G. Ramage.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner, London, S.W.—At Large Lecture Theatre, Jan. 27, 4.30 p.m. Lecture-demonstration: "*Neurology*."

UNIVERSITY COLLEGE LONDON.—At Anatomy Theatre, Gower Street, London, W.C., Jan. 27, 1.15 p.m. "*Some Modern Views on Evolution*," by Professor J. B. S. Haldane.

Friday

KENT AND CANTERBURY HOSPITAL, Canterbury.—Jan. 28, 5 p.m. to 7 p.m. Clinical meeting.

LONDON CHEST HOSPITAL, Victoria Park, E.—Jan. 28, 5 p.m. "*Extrathoracic Pain in Cardiovascular Disease*," by Dr. J. L. Lovibond.

MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES, 11, Chandos Street, London, W.—Jan. 28, 8 p.m. General meeting. "*Modern Interpretations of Serum Tests*," by Dr. I. N. Orpwood Price.

NORTH OF ENGLAND SOCIETY OF ANAESTHETISTS.—At Royal Victoria Infirmary, Newcastle-upon-Tyne, Jan. 28, 7.30 p.m. Third meeting. "*Dental Anaesthesia*," by Dr. Bernard Johnson.

ROYAL MEDICAL SOCIETY, 7, Melbourne Place, Edinburgh.—Jan. 28, 8 p.m. Debate.

UNIVERSITY COLLEGE LONDON: DEPARTMENT OF PHARMACOLOGY.—At Physiology Theatre, Gower Street, London, W.C., Jan. 28, 5.15 p.m. "*The Relationship Between Physico-chemical Properties of Drugs and Their Pharmacological Activities*," by Dr. F. Bergel, Ph.D.

Saturday

NORTH OF ENGLAND OTOLARYNGOLOGICAL SOCIETY.—At Eye and Ear Infirmary, Myrtle Street, Liverpool, Jan. 29, 2 p.m. Clinical meeting.

APPOINTMENTS

CASSON, F. R. C., M.B., D.P.M., Clinical Assistant, Department of Psychological Medicine, King's College Hospital, Denmark Hill, London, S.E.

COWAN, KENNETH, M.D., D.P.H., County Medical Officer and School Medical Officer for Essex.

FOGARTY, T. N., M.B., B.Ch., D.M.R.E., Consultant Radiologist, Lurgan, Banbridge, Portadown, Dungannon, and Armagh City Hospitals.

FRASER, JOHN, M.B., Ch.B., Medical Superintendent, Edinburgh Convalescent Hospitals Group, Scottish South-Eastern Regional Hospital Board.

HARVEY, F. C. B., M.R.C.S., L.R.C.P., Full-time Medical Officer of Health for District No. 9 (including Abergavenny Borough and Rural areas), Welsh Board of Health.

HILDITCH, J. HAWORTH, M.B., Ch.B., D.P.H., Medical Officer for Wigan.

HOSPITAL FOR SICK CHILDREN, Great Ormond Street, London, W.C.—*House-physicians*, M. G. Philpott, M.B., B.S., M.R.C.P., H. J. W. Fisher, M.B., B.S., M.R.C.P. *House-surgeon*, M. E. Larg, M.R.C.S., L.R.C.P., D.R.C.O.G. *Medical Registrar and Pathologist*, S. D. V. Weller, M.D., M.R.C.P. *Registrar to the Department of Psychological Medicine*, R. Meyer, M.B., B.Ch., M.R.C.P.

HURFORD, J. V., M.D., M.R.C.P., D.P.H., Physician-Superintendent, King George V Sanatorium, Godalming, Surrey.

LONGBOTTOM, DONALD, M.B., Ch.B., D.P.H., Divisional Medical Officer and Medical Officer of Health to the Altrincham Division, Cheshire County Council.

OWEN, EVELYN D., M.B., B.S., D.P.H., Full-time Medical Officer to Cwmbran and Caerleon Urban Districts (Area No. 8), Monmouthshire.

SILVERTON, M. I., M.R.C.S., L.R.C.P., Medical Officer of Health, Battle Rural District, Sussex.

SOUTH-WESTERN REGIONAL HOSPITAL BOARD.—The following appointments are announced: J. A. Pitt Evans, M.B., B.S., Pathologist, Cheltenham General Hospital; N. R. W. Simpson, M.B., B.S., Director of Physiotherapy, North Gloucestershire Group of Hospitals.

TATTERSALL, P. E. R., M.D., M.R.C.P., Physician, Tyrone County Hospital, Omagh, under Northern Ireland Health Service.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Lee.—On Jan. 7, 1949, at Liverpool Maternity Hospital, to Hazel (née Green), wife of Dr. David Lee, 1, Storrsdale Road, Liverpool, a son.

Mansour.—On Jan. 4, 1949, at Liverpool Maternity Hospital, to Enid Eileen (née Huston), wife of Dr. Joseph Mansour, a son.

O'Hagan.—On Dec. 23, 1948, to Dorothy (née Pledge, M.B., B.S.), wife of Stanley A. O'Hagan, M.B., B.S., D.P.H., of Winteringham, Scunthorpe, a son—Michael Stanley.

Ritchie.—On Jan. 13, 1949, at Edinburgh, to Professor Anthony and Dr. Elizabeth Ritchie, University of St. Andrews, a son.

Rosser.—On Dec. 25, 1948, at the Birmingham Maternity Hospital, to Peggy (née Dash, M.B., B.S.), wife of Brinley M. Rosser, a son.

DEATHS

Bainbridge.—On Jan. 8, 1949, suddenly, Dr. Matthew McLintock Bainbridge, of 316, Monument Road, Birmingham. Dearly loved husband of Eva and second son of the late Reverend Philip and Mrs. Bainbridge, of Makerstoun, Kelso.

Barker.—On Jan. 11, 1949, at 3, Randolph Place, Edinburgh, Duncan McFarlan, Barker, M.B., Ch.B.

Blake.—On Jan. 10, 1949, at 6, Regent Road, Great Yarmouth, Valentine Henry Blake, M.B., B.S.

Denmark.—On Jan. 10, 1949, Alexander George Denmark, M.D., of Burleigh, Bishopsteignton, Devon.

Foggie.—On Jan. 13, 1949, at Dundee Royal Infirmary, William Edward Foggie, D.S.O., M.D., F.R.C.P.Ed.

Graham.—On Jan. 2, 1949, Thomas Graham, M.C., M.B., Ch.B., of 46, Cranston Avenue, Bexhill, aged 72.

Grant.—On Jan. 11, 1949, John Wemyss Grant, M.B., C.M., D.P.H., Lieutenant-Colonel, I.M.S., retired, of 29, Carlton Avenue, Broadstairs, Kent, aged 79.

Hewitt.—On Dec. 28, 1948, at Canford Lane, Bristol, John Hewitt, L.R.C.P.&S.I. and L.M., of Cwedon Road, Weston-super-Mare, aged 73.

Hodgson.—On Jan. 2, 1949, at 162, Northway, Maghull, Liverpool, Albert Ernest Hodgson, M.D., D.P.H., aged 68.

Holthouse.—On Jan. 2, 1949, Edwin Hermus Holthouse, F.R.C.S., of 6, Gilbert Road, Ramsgate, formerly of 1, Park Crescent, London, W., aged 93.

Hutchinson.—On Jan. 11, 1949, at Bournemouth, Leslie Thomason Rose Hutchinson, M.D., D.P.H., Lieutenant-Colonel, I.M.S., retired.

Leach.—On Jan. 9, 1949, at Royal Northern Infirmary, Inverness, William John Leach, M.B., Ch.B., of Eilleandonan, Beauly, Inverness-shire.

Lees.—On Jan. 10, 1949, Edwin Leonard Lees, M.D., of Clifton, Bristol, aged 85.

MacLaren.—On Jan. 6, 1949, at 10, Scarsdale Villas, London, W., James Alexander MacLaren, M.B., C.M.Ed., aged 89.

Messer.—On Jan. 1, 1949, Andrew William Messer, M.B., C.M.Ed., J.P., of Lemington-on-Tyne, Northumberland, aged 82.

Nicol.—On Jan. 7, 1949, at a Bournemouth nursing home, Alexander Campbell Nicol, M.R.C.S., L.R.C.P., formerly of Springfield Crescent, Parkstone, Dorset, aged 76.

Rees.—On Nov. 21, 1948, Thomas Rogers Rees, M.R.C.S., L.R.C.P., of Cardiff, aged 56.

Russell-Cargill.—On Jan. 7, 1949, at 162, Ashley Gardens, London, S.W., James Alexander Russell-Cargill, M.B., Ch.B.Ed.

Rust.—On Dec. 10, 1948, at Graham Road, Malvern, Worcs, James Rust, M.D., aged 79.

Sadlier.—On Jan. 5, 1949, at Masterton, New Zealand, Horace William Sadlier, M.B., B.Ch.

Sands.—On Jan. 6, 1949, at his home, Gringley-on-the-Hill, Doncaster, Howard Sands, M.B., B.Ch., late of Chapeltown, Sheffield, aged 83.

Watt.—On Jan. 2, 1949, at Perth Royal Infirmary, John Watt, L.R.C.P.&S.Ed., L.D.S., of St. Margarets, Muthill, Perthshire, eldest son of the late J. W. I. Watt, Glasgow.

Wild.—On Jan. 6, 1949, at New End Hospital, London, N.W., Granville Burnett Wild, M.B., Ch.B., Lieutenant-Colonel, R.A.M.C., aged 57.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Home-cured Tobacco and Amblyopia

Q.—*Is there any evidence to support the suggestion that the smoking of home-cured tobacco may lead to tobacco amblyopia more readily than the smoking of tobacco cured commercially?*

A.—Before any attempt is made to guess at the possible results of the use of home-cured tobacco, it may be as well to consider the factors generally accepted as leading to tobacco amblyopia. This is due to a breakdown in tolerance to nicotine and occurs when the intake of toxic substances exceeds the capacity of the liver to deal with them. The problem concerns the functions of the liver, and especially its formation of glycogen, in addition to the local reaction in the eye. Schepens was able to observe a large number of cases in Belgium during the recent war (*Trans. ophthal. Soc. U.K.*, 1946, **66**, 309). He found that tobacco amblyopia, a rarity before the war, had increased about ten times. Several factors must be considered in each case—type of tobacco, alcohol consumption, food deficiency, and mental strain.

Tobacco as sold commercially has a small nicotine content owing to the breakdown of that substance by fermentation during the process of curing. In "green" tobacco the fermentation has not been completed and the percentage of nicotine is high. The stalks and ribs are more toxic than the leaf, and so, if they are not to be removed, they must be well crushed and broken up to allow of better fermentation. It was found in Belgium during the war that a poor quality of tobacco, as judged by the smoker, need not be as toxic as an apparently better tobacco. It was also found that the home-grown leaf was responsible for more cases of amblyopia than the commercial brands. In the past it has been taught that a high consumption of alcohol, especially spirits, predisposes to amblyopia. The pendulum is now swinging in the opposite direction, and many assert that alcohol has little or no influence in making the eyes more susceptible. Food deficiencies, especially in proteins and fats, are definitely in the picture. Many cases of amblyopia were seen by Dr. Wecker in the Siege of Paris in 1870, and the numbers were found to be increased in Germany after the 1914–18 war. With such deficiencies recovery is slower and sometimes minor lesions are to be detected in the fundus. Despite the prominent position of vitamins in the dietary, a reduced intake probably has no influence at all on the occurrence of tobacco amblyopia. Mental strain seems to increase susceptibility to the disease, and this was obviously present during the Siege of Paris, in Germany during the war of 1914–18, and in Belgium in the last war. It may have an effect *per se*, or lead to a greater consumption of tobacco in order "to soothe the nerves" and allay hunger.

Amblyopia is most prevalent between the ages of 55 and 60, but under the adverse conditions listed above cases have been recorded at 30. The lesion is now considered to be primarily in the retina itself, the optic nerve being only secondarily affected at a late stage. Cure of the condition usually confers immunity, and recurrence is rare. To sum up, home-grown tobacco need not be toxic and produce tobacco amblyopia if it is properly fermented and cured before use. The danger, however, is greatly enhanced if there is any dietary deficiency or excessive mental strain.

Threatened Abortion

Q.—(*a*) *Has progesterone any place in the treatment of threatened abortion in the absence of facilities for a pregnanediol excretion test?* (*b*) *Please recommend the routine most likely to be successful in preventing abortion when a woman, three months pregnant and with no apparent abnormality, starts to bleed.*

A.—(*a*) There is still some dispute, but the evidence so far available suggests that progesterone should not be given indiscriminately to all cases of threatened abortion. Only about 40% of cases show evidence of progesterone deficiency as determined by pregnanediol excretion tests, and the administration of progesterone to the others may encourage abortion. Therefore the overall results for any large series of cases are probably better if progesterone is not used at all.

(*b*) The most important part of treatment is complete rest in bed, and that for at least a further seven days after all bleeding has ceased. This may be supplemented, at any rate in the initial stages, with morphine or such sedatives as the bromides or phenobarbitone. If possible, arrangements should be made for a biological test for pregnancy and for a pregnanediol estimation to be carried out on a first morning specimen of urine, and progesterone therapy should be withheld until the result is available. Synthetic vitamin E, 30 mg. thrice daily, appears to help sometimes and can do no harm. After the symptoms have settled down the patient needs to live a restful life, avoiding coitus and travelling, and she may continue to take vitamin E.

Combined Pertussis Vaccine and Diphtheria Prophylactic

Q.—*There seems to be some difference of opinion about the combined injection of pertussis vaccine and A.P.T. Is there any contraindication? The anti-pertussis vaccine is sometimes given at monthly and sometimes at weekly intervals. Which do you advise, and why?*

A.—The main objection at present to the combination of a pertussis vaccine with diphtheria prophylactic is that we still cannot tell whether any particular pertussis vaccine will prove an effective immunizing agent or not. If, therefore, a poor pertussis antigen is combined with A.P.T. its failure to protect children against whooping-cough may adversely affect the attitude of parents to diphtheria immunization and they may decide that prophylactic injections in general are of little value. Another objection is that immunization against whooping-cough should be begun as early in life as possible, say at 3 months, since infections may occur early and are most severe in infancy. On the other hand, diphtheria prophylactic is more useful and probably more effective if given towards the end of the first year of life.

The optimum dosage or interval of injection with pertussis vaccines is still not known. There is some evidence that a better antibody response is obtained by injections at three- or four-week intervals than by weekly injections, and the present tendency is to give two or three injections of 10,000 million to 30,000 million organisms at monthly intervals. The combination of pertussis vaccine with diphtheria prophylactic has no inhibitory effect on the antibody response to either antigen; indeed, the antitoxin response to diphtheria prophylactic is usually enhanced when a combined antigen is used.

Intravenous Iron

Q.—*What is the present opinion of parenteral iron preparations? What are the methods of use and dosage? I have a woman patient, aged 27, who has a severe iron deficiency anaemia which responds rapidly to iron therapy. Unfortunately, in spite of trial of every oral form of iron, she shows a marked intolerance to this treatment, which causes abdominal pain and diarrhoea whenever it is given. Her haemoglobin level is now about 50%.*

A.—Intramuscular injections of iron are not widely used in Britain, as an adequate amount cannot be given without risk of toxic symptoms and the injections tend to be painful. Nissim (*Lancet*, 1947, **2**, 49) reported the use of intravenous saccharated iron oxide. The commercial preparation "ferrivenin" is now available for the treatment of hypochromic anaemias which prove refractory to oral therapy. Each 5-ml. ampoule contains 100 mg. of elemental iron as an iron-sucrose preparation, and it is claimed that there is "100% utilization" of such iron as compared with about 14% for ferrous sulphate and 1.5–3.0% for ferri et ammon. cit. taken by mouth. A test dose of 1.5 ml. is injected intravenously on the first day, 3 ml. on the second, and subsequently 5 ml. or 10 ml. either daily or on alternate days until a "satisfactory response" is obtained. Intravenous injections should be carefully performed, and it is important to prevent any of the iron solution escaping into the tissues.

Reactions—for example, malaise, pain in the back, etc.—may occur, but are uncommon. When injections are given slowly (about 2 ml. a minute) venous thrombosis does not often take place and no "washing through" of the needle with glucose saline is necessary. As 25 mg. of iron are calculated to raise the haemoglobin 1% it is reckoned that each ampoule should increase the haemoglobin by about 4%. A large infusion of 5% glucose with 2% ferrivenin has been suggested in order to avoid repeated venupuncture. Further reports of the latter technique are awaited. In the case mentioned, intravenous iron would seem well worthy of trial. In every case of so-called refractory iron deficiency anaemia, however, it is all-important to make sure that the anaemia is not secondary to such conditions as reticulosis, neoplasm, or nephritis, and that there is no evidence of blood loss.

Fat Intolerance

Q.—*A man of 56 is very intolerant of fat, and it is thought that recurrent infections may be due to too low a vitamin A intake. All the usual preparations of vitamin A cause digestive disturbances. Could carotene be given instead? Is it unwise, in general, to give vitamin D in concentrated form to elderly people?*

A.—There is no evidence that recurrent infections in man are due to a low intake of vitamin A. If it is desired to give this patient supplements of vitamin A, liquid vitamin A conc., *B.P.*, may be administered in daily doses of 1½ minims (0.09 ml.). This is suspended in oil, but surely so small an amount would be tolerated. In any case, it could be administered in food without the patient's knowledge. Carotene can be given instead, if necessary, in the form of tablets containing 4,500 units (daily requirement, 4,000 units). Actually carotene is equivalent to just over half its weight of vitamin A, so that the dose would be two tablets daily. Carotene is absorbed from the gut and converted into vitamin A in the body. There is no objection to old persons taking vitamin D concentrates, provided they do not take more than approximately 800 units daily. Why not give the patient a combined preparation of vitamins A and D? There are preparations available 1 minim (0.06 ml.) of which contains a day's requirements of vitamins A and D.

Ammoniacal Dermatitis in Infants

Q.—*What causes ammoniacal urine and the associated dermatitis in babies, and what can be done to prevent it?*

A.—There are two main theories about ammoniacal dermatitis in infants. The first is that a urea-splitting ferment in the napkins sets free ammonia. Hence the treatment is to kill the ferment by boiling the napkins after soaking them in perchloride of mercury solution overnight, and to apply soothing powders or calamine lotion to the inflamed skin. The other view is that ammonia is set free by the action of soda in the napkins upon combined ammonia salts in the urine. If excessive acid bodies are being passed as a result of fever or too much fat in the diet, then there is more combined ammonia in the urine as the outcome of a renal compensatory mechanism, with a greater chance of ammonia being liberated. Here it is important to reduce fat in the dietary, to give alkalis by mouth, such as citrate 5 to 10 gr. (0.32 to 0.65 g.) three times a day, and to use boric powder freely in the napkin area to mop up free ammonia. If the dermatitis in boy babies goes far enough to produce a meatal ulcer, then boric ointment should be applied. Either theory or both may be correct. Experience in welfare-centre work suggests that adoption of the second view gives better practical results as a working basis.

Insulin Sensitivity

Q.—*A woman aged 75 suffers pain on injection of protamine zinc insulin, and subsequently reddened, indurated, tender swellings appear at the sites of injection. Bacterial contamination has been excluded. I am informed that all brands of insulin now come from a common "pool." If this is the case, is there any other form of insulin that can be tried?*

A.—The varieties of insulin available differ to some extent, since the processes of extraction from the pancreas and methods of purification are not identical. As one brand of protamine zinc insulin is causing local reactions, the two others should be tried and the one which gives the least reaction persevered with. The swellings will probably soon disappear, but if they do not the method of desensitization outlined in the answer to the question on sensitivity to insulin (*British Medical Journal*, Sept. 20, 1947, p. 475) should be adopted.

Athlete's Foot

Q.—*It has been reported to me that there was an increase of athlete's foot last summer and that the persons affected had attended the public swimming-baths. Now it is winter, what is the best way to disinfect the duck-boards, as they appear to be a possible source of infection? What would be the best way to disinfect them in the summer, apart from scrubbing them with soap and water daily?*

A.—It is doubtful if duck-boards, etc., are a very serious source of infection, but in winter a thorough treatment with formalin would probably be wise, followed by scrubbing with soap and water. This measure could also be employed occasionally in the summer.

NOTES AND COMMENTS

Leukoplakia and Kraurosis Vulvae.—Mr. STANLEY WAY (Newcastle-upon-Tyne) writes: In "Any Questions?" (Dec. 4, 1948, p. 1005) your writer gave a brief and concise account of kraurosis and leukoplakia of the vulva, and, in giving the incidence of the association of carcinoma of the vulva with leukoplakia, quoted along with the figures of Bonney and Taussig my own findings as published in my recent Hunterian Lecture to the Royal College of Surgeons. In your issue of Jan. 1 (p. 42) Dr. Elizabeth Hunt states that when cancer occurs in association with leukoplakia it is found on the internal surface of the vulva only, and from this she concludes that excision of the vulval skin is not justified. This statement is completely erroneous. I cannot give the exact figures for my last 100 cases, but I can state with certainty that in the last 20 cases of cancer of the vulva which I have treated and in which leukoplakia existed the external surface of the vulva was affected by tumour in every one. In six both the external and internal surfaces were involved with tumour, and only in two was the tumour confined to the mucous surface, but this was extensively affected by leukoplakia. Is Dr. Hunt not aware that both the skin and the mucous surfaces can be affected by this disease? I think it is probable that some cases of leukoplakia of the vulva may never become malignant, but there is absolutely no means of telling which are which, and therefore I feel most strongly that immediate excision of the leukoplakic vulva is the right and proper treatment. Cancer of the vulva is one of the very few examples of malignant disease in which prophylactic treatment can be applied with a fair measure of success. It seems a pity then that your readers should have doubts about this put before them by such an authority as Dr. Hunt. Finally, whilst I would agree with Dr. Hunt that there are lesions of the vulva which are wrongly called leukoplakia, there are far more lesions which are given high-sounding names by dermatologists but which are in fact the disease which less ambitious gynaecologists are content to call leukoplakia.

Rh Factor and Pregnancy.—Dr. S. A. DOXIADIS (Sheffield) writes: In "Any Questions?" (Jan. 1, p. 42) it is stated that in the presence of Rh antibodies in the mother's blood the infant should be transfused "without delay if its cells are found to be sensitized to Coombs's test." May I suggest that unless the writer had in mind replacement transfusion his advice is contrary to the opinion of many experienced workers? To give an ordinary transfusion to an infant before it becomes anaemic is unjustified and potentially dangerous. It is further stated that "there is little or no danger to the first foetus from this cause (presumably haemolytic disease of the newborn) unless in twin pregnancy." As far as I am aware twins are not more likely to be affected by this disease than single foetuses either in the first or subsequent pregnancies. Should there be any evidence for such a likelihood a reference to it would be much appreciated.

Correction.—In the note in "Books Received" (Jan. 15, p. 104) on *Cardiology* by Dr. W. Evans, we should have stated that his book is intended for postgraduate students and medical practitioners as well as medical students.

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